Studies on Pentamethylcyclopentadiene in Organic Synthesis(Dissertation_全文)

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Contents

Introduction and General Summary

Cp*-Metal Complexes

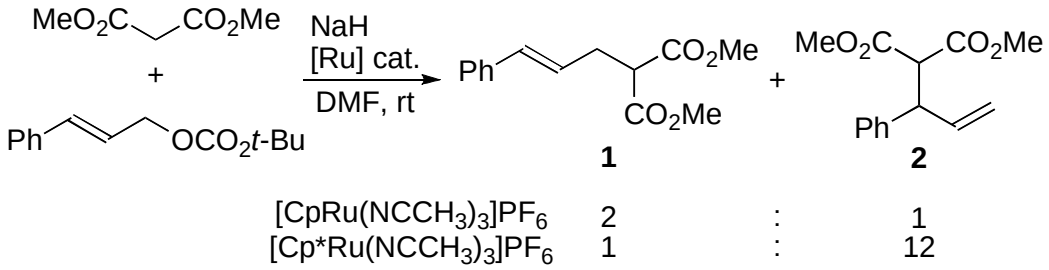
Pentamethylcyclopentadienyl (C_5Me_5, Cp*) ligand is indispensable in transition metal chemistry since the first Cp*-metal complex was discovered accidentally in 1962 (Scheme 1).[1] The delocalized 6π-electron system and its steric bulkiness provide coordinated metals with a unique environment.

Scheme 1. First Synthesis of Cp*-metal complex

The Cp* ligand is strongly electron-donating. The electron density at the metal centers increases by coordination of the Cp* ligand to transition metals, and Cp*-metal complexes become more reactive to oxidative addition.

Introduction of the Cp* ligand affects the selectivity of reactions. Due to the steric repulsion between the Cp* ligand and substrates, reactions proceed with high selectivity. For instance, the reaction of Boc-protected cinnamyl alcohol with dimethyl malonate in the presence of a catalytic amount of $[CpRu(NCCH_3)_3]PF_6$ gives a mixture of **1** and **2** by a ratio of 2 : 1. Interestingly, the reaction with $[Cp^*Ru(NCCH_3)_3]PF_6$ produces **2** as a major product (Scheme 2).[2]

Scheme 2. Ruthenium-Catalyzed Allylic Alkylation



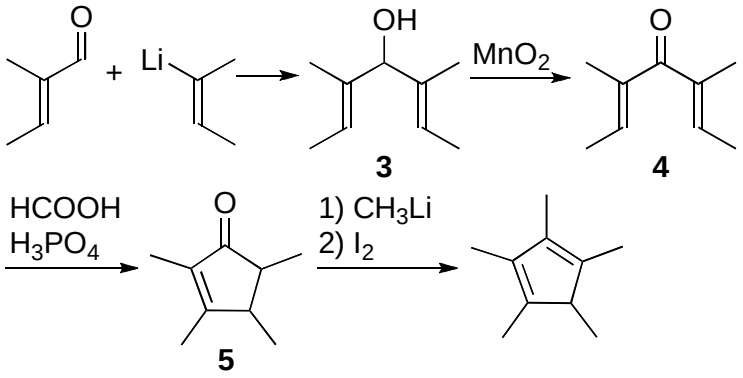
The Cp* ligand also provides transition metals with interesting reactivity, enhanced solubility, stability and crystallizability.

Synthesis of Pentamethylcyclopentadiene

Pentamethylcyclopentadiene (C_5Me_5H, Cp*H) is a precursor of Cp*-metal complex. The development of large-scale synthesis of Cp*H is important for transition metal chemistry. Pentamethylcyclopentadiene Cp*H has a quite simple structure; nevertheless, it took a long time to find its practical synthetic method.

de Vries reported the first synthesis of Cp*H (Scheme 3).[3] Nucleophilic attack of (*Z*)-2-lithio-2-butene to tiglaldehyde gave an alcohol **3**. Oxidation of **3** provided a ketone **4**. Nazarov ring closure of **4** gave cyclopentenone **5**. The reaction of **5** with methyllithium, followed by dehydration provided Cp*H. This method was expensive and tedious. Progress of Cp*-metal chemistry was hence severely hampered.

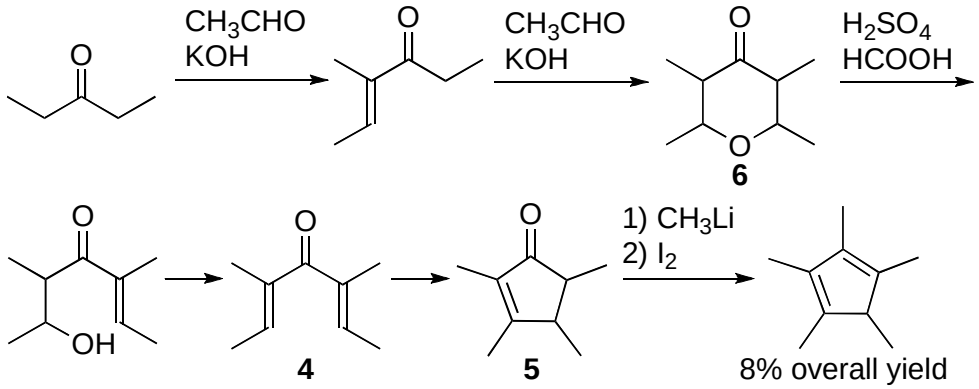
Scheme 3. First Synthesis of Cp*H



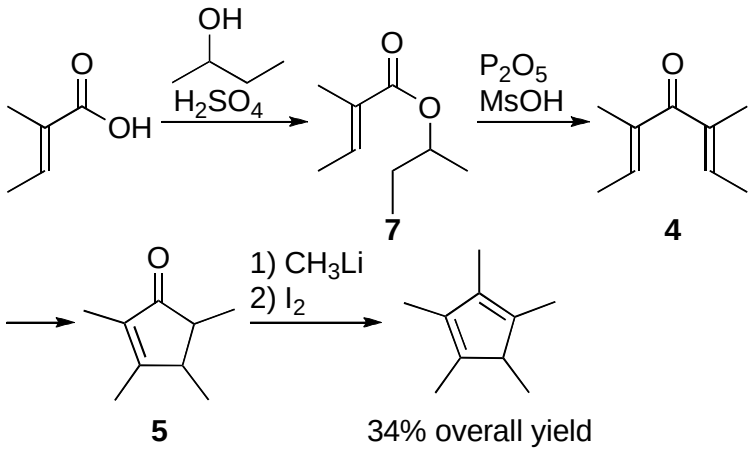
Burger and Whitesides developed methods for the synthesis of Cp*H with cheap starting materials. Burger reported a procedure starting from 3-pentanone and acetaldehyde. The reaction of 3-pentanone with acetaldehyde in the presence of potassium hydroxide produced γ-pyrone **6**. Acid-mediated ring opening of **6** and dehydration, followed by Nazarov ring

closure provided **5** (Scheme 4).[4] Whitesides reported the synthesis with tiglic acid. Treatment of tiglic acid with 2-butanol gave an ester **7**. Cyclization of **7** *via* **4** provided **5** (Scheme 5).[5] Unfortunately, their methods provided the desired Cp*H in only 8% and 34% overall yields, respectively.

Scheme 4. Burger's Method

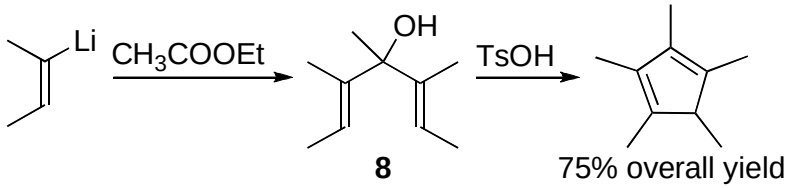


Scheme 5. Whitesides's Method



A major breakthrough was achieved by Bercaw. Nucleophilic addition reaction of (*Z*)-2-lithio-2-butene to ethyl acetate gave an alcohol **8**, which was dehydrated and cyclized to Cp*H (Scheme 6).[6] This method is now the best way to prepare Cp*H.

Scheme 6. Bercaw's Method

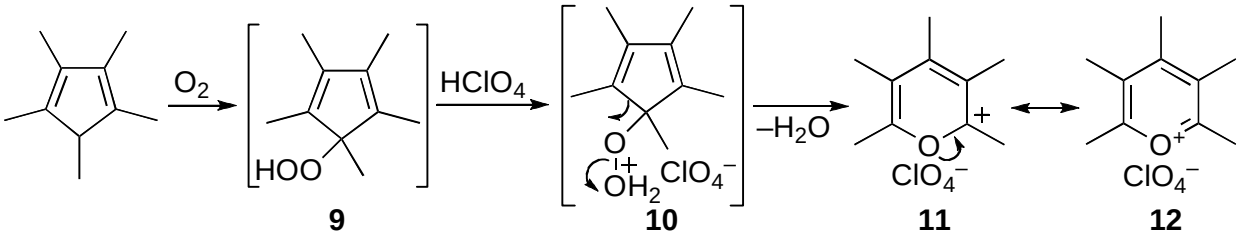


Reactivities of Cp*H and its Derivatives

The chemistry of Cp*-metal complexes and synthesis of Cp*H have been studied for more than forty years. In addition, the reactivities of Cp*H have been also studied.

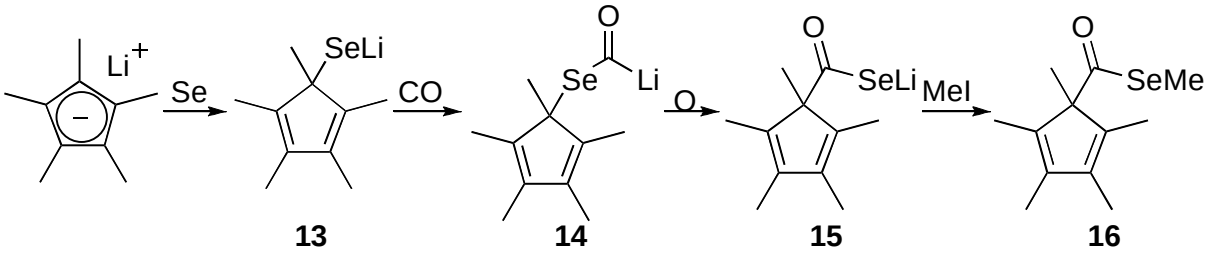
Oxidation of Cp*H by molecular oxygen in the presence of $HClO_4$ afforded pyrylium cation **12** (Scheme 7).[7] The bis-allylic hydrogen in Cp*H undergoes an oxidation reaction forming hydroperoxide **9**, since the bis-allylic hydrogen is more reactive and more vulnerable to oxygen attacking than hydrogens of methyl groups. The hydroperoxide generates cation **10** after protonation, and successive O–O bond cleavage and C–O bond formation provide **12**.

Scheme 7. Synthesis of Pyrylium Cation



The carbonylation of **13** with CO followed by treatment with iodomethane leads to the formation of selenol ester **16** (Scheme 8).[8] Reaction of Cp*Li with selenium affords **13**, which then reacts with CO to give selenocarboxylate **15** *via* rearrangement of **14**. Selenol ester **16** is formed by trapping of **15** with methyl iodide.

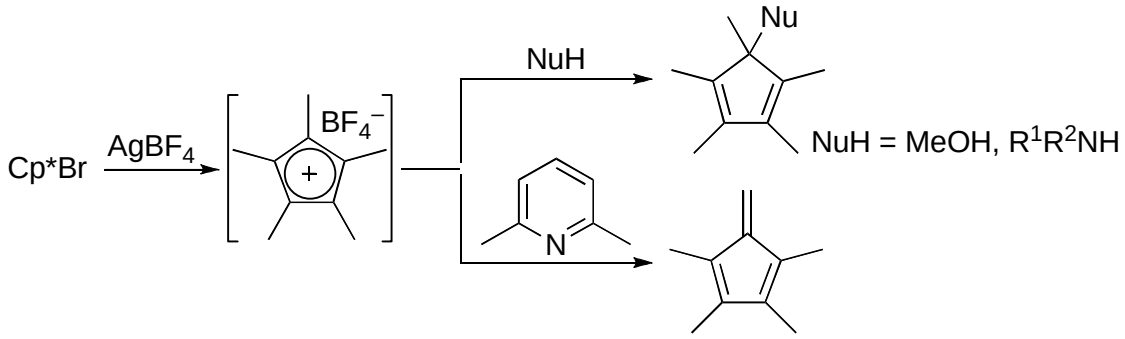
Scheme 8. Synthesis of Selenol Ester



13 **14** **15** **16**

Treatment of Cp*Br with $AgBF_4$ provides pentamethylcyclopentadienyl cation (Cp^{*+}), which can be trapped by different nucleophiles (Scheme 9).[9] Pentamethylcyclopentadienyl cation Cp^{*+} reacts with methanol to give 1-methoxy-1,2,3,4,5-pentamethyl-2,4-cyclopentadiene. In the presence of amines, the corresponding pentamethylcyclopentadienyl-substituted amines are formed. The reaction of Cp^{*+} with sterically crowded amines leads to tetramethylfulvene.

Scheme 9. Reactivities of Cp^{*+}

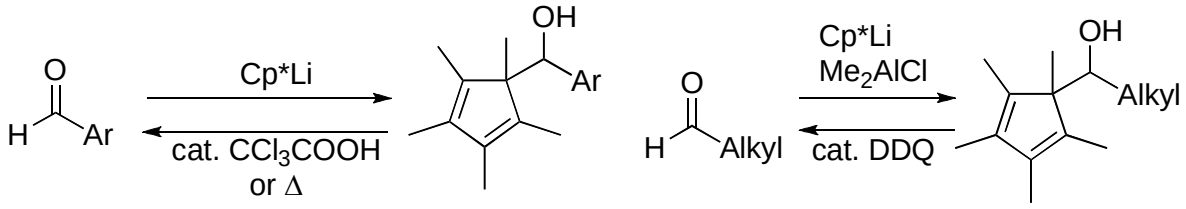


Summary of Thesis

Pentamethylcyclopentadiene Cp*H is used extensively as the precursor of Cp* ligand of transition metal complexes. However, the study on Cp*H as a reagent in organic synthesis is rare. Then the author has been exploring utilities of Cp*H and developing new reactions. He found three applications: transformation through carbon–Cp* bond formation and cleavage (Chapter 1–3), development of $Cp^*CH_2PPh_2$ ligand (Chapter 4), and Cp*Li as a base (Chapter 5).

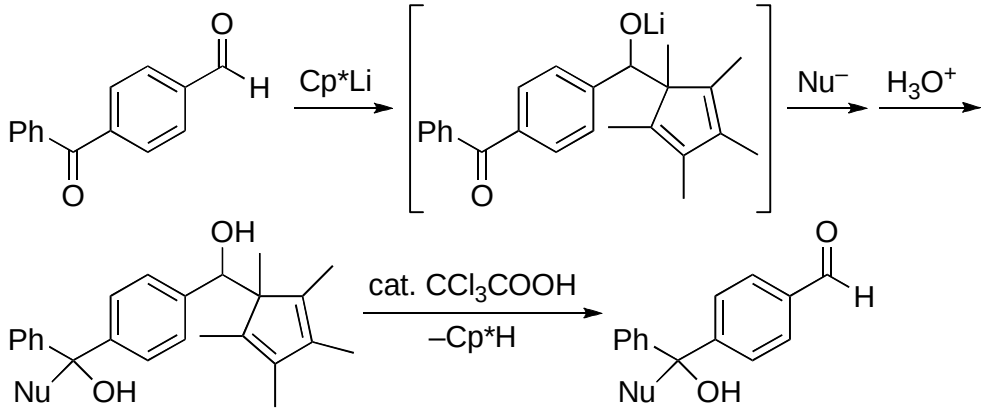
In Chapter 1, the author describes nucleophilic addition of Cp*Li to aromatic aldehydes and carbon–Cp* bond cleavage of the adducts affording the parent aldehydes (Scheme 10).[10a,10c] The reaction of aromatic aldehydes with Cp*Li provided the corresponding alcohols. The alcohols were unstable under acidic conditions and were transformed into the parent aldehydes *via* carbon–Cp* bond cleavage. Heating the alcohols also provided the parent aldehydes. He also illustrates Me_2AlCl-promoted nucleophilic addition of Cp*Li to aliphatic aldehydes and DDQ-mediated carbon–Cp* bond cleavage of the adducts providing the parent aldehydes (Scheme 10).[10b,10c] The reaction of aliphatic aldehydes with Cp*Li gave the alcohols in low yields, because Cp*Li works as a base to generate lithium enolates. He found that treatment of aliphatic aldehydes with Cp*Li in the presence of Me_2AlCl provided the corresponding alcohols. In contrast to the alcohols derived from aromatic aldehydes, the alcohols generated from aliphatic aldehydes are stable under acidic conditions or at high temperature. He discovered that the reaction of the alcohols with a catalytic amount of DDQ leads to the cleavage of the carbon–Cp* bond to yield the parent aliphatic aldehydes and Cp*H.

Scheme 10. Formally Reversible Addition of Cp*Li to Aldehydes



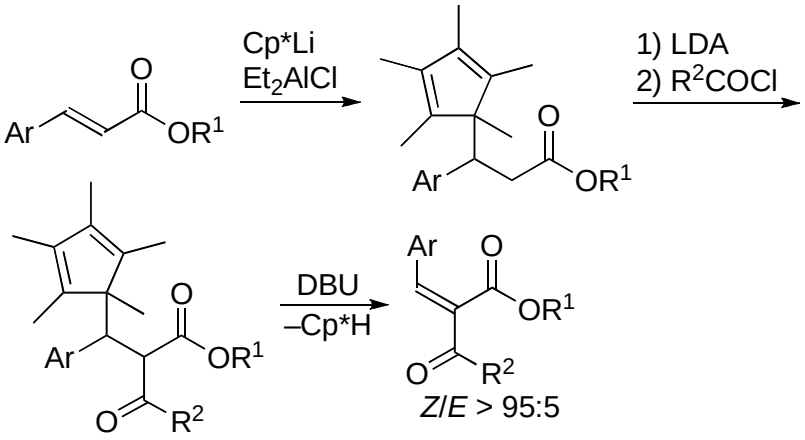
The author found that carbon–Cp* bond formation and cleavage sequence is applicable to *in situ* protection of aldehydes (Scheme 11).[10a,10c]

Scheme 11. Utility of Cp* Group as a Protective Group of Aldehydes



In Chapter 2, the author illustrates acylation of cinnamate esters through carbon–Cp* bond formation and cleavage (Scheme 12).[11] Conjugate addition of Cp*Li to (*E*)-cinnamate esters in the presence of Et_2AlCl gave 1,4-adducts. The adducts underwent α-acylation and elimination of Cp*H to provide (*Z*)-*α*-acylcinnamate esters.

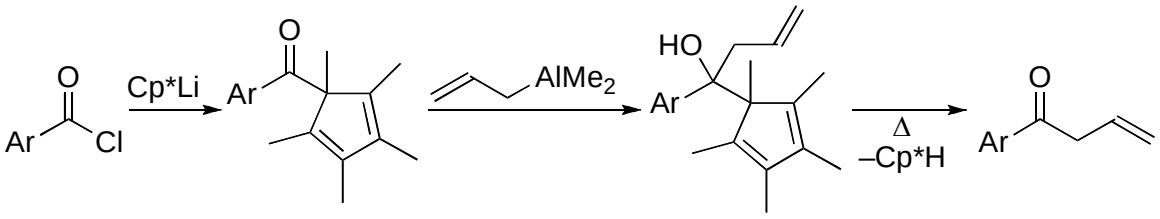
Scheme 12. Synthesis of (*Z*)-α-Acylcinnamate Esters



In Chapter 3, synthesis of β,γ-unsaturated ketones through carbon–Cp* bond formation

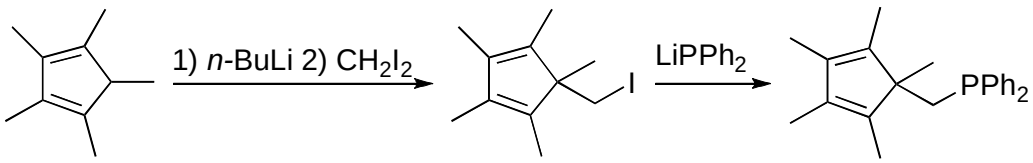
and cleavage is disclosed (Scheme 13).[12] Aryl pentamethylcyclopentadienyl ketones, which are prepared from acid chlorides with Cp*Li, underwent allylation with allylaluminum reagent to yield the corresponding alcohols. Heating the alcohols in boiling toluene resulted in removal of Cp*H to provide β,γ-unsaturated ketones.

Scheme 13. Synthesis of β,γ-Unsaturated Ketones



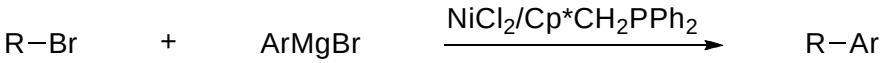
In Chapter 4, author describes the development of a new ligand $Cp^*CH_2PPh_2$, a monophosphine ligand with pentamethylcyclopentadienyl group.[13] The phosphine could be synthesized in short steps (Scheme 14).

Scheme 14. Synthesis of $Cp^*CH_2PPh_2$



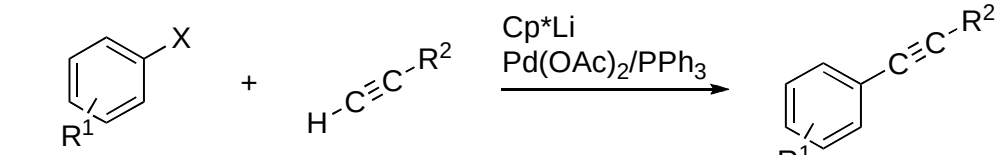
Cross-coupling reactions of organometallic reagent with alkyl halides are difficult, since alkylmetal complexes are prone to undergo β-hydride elimination.[14] The author expected that both phosphine and the diene of Cp* could occupy vacant coordination sites necessary for the β-hydride elimination. He found that nickel-catalyzed reaction of alkyl halides with aryl Grignard reagents afforded the cross-coupling products in good yields by using $Cp^*CH_2PPh_2$ as a ligand (Scheme 15).

Scheme 15. Nickel-Catalyzed Cross-Coupling Reaction of Alkyl Halides with Aryl Grignard Reagents in the Presence of $Cp^*CH_2PPh_2$ Ligand



In Chapter 5, the author illustrates the use of Cp*Li as a base: application to palladium-catalyzed cross-coupling reaction of aryl-X or alkenyl-X (X = I, Br, OTf, ONf) with terminal acetylenes (Scheme 16).[15] Although many kinds of alkynylmetals have been used for palladium-catalyzed cross-coupling reaction of aryl-X or alkenyl-X,[16] the reaction with lithium acetylides is difficult. The reaction of a palladium catalyst with an excess amount of lithium acetylides provides lithium palladate, which does not exhibit any catalytic activity.[17] He thought that gradual formation of lithium acetylides would avoid the formation of the inactive lithium palladate. He found that the reaction of aryl-X or alkenyl-X (X = I, Br, OTf, ONf) with terminal acetylenes in the presence of a catalytic amount of palladium provided the alkynylated products in good yields by using Cp*Li as a base.

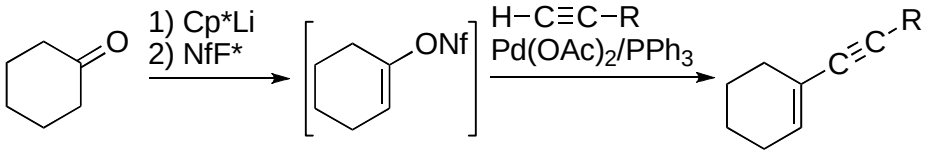
Scheme 16. Palladium-Catalyzed Cross-Coupling Reaction of Aryl Halides with Terminal Acetylenes using Cp*Li



X = I, Br, OTf, ONf

The author also found that Cp*Li can be used as a bulky base to prepare lithium enolates. With this reactivity, he accomplished one-pot synthesis of enynes from ketone in good yields (Scheme 17).[15]

Scheme 17. One-Pot Synthesis of Enynes from Ketones



*NfF = 1,1,2,2,3,3,4,4,4,-nonafluoro-1-butanesulfonyl fluoride

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Abbreviations

Ac	acetyl
Ar	aryl
Boc	*t*-butoxycarbonyl
Bu	butyl
c	cyclo
˚C	degrees Celsius
ca.	about
calcd	calculated
cat.	catalytic
Co.	company
COSY	correlation spectroscopy
Cp*H	1,2,3,4,5-pentamethyl-1,3-cyclopenta-diene
Cp*	pentamethylcyclopentadienyl
Cp	cyclopentadienyl
δ	chemical shift in parts per million downfield from tetramethylsilane
d	doublet (spectral)
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DDQ	2,3-dichloro-5,6-dicyanobenzoquinone
DEPT	distortionless enhancement by polarization transfer
DABCO	1,8-diazabicyclo[2.2.2]octane
DME	dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
Ed(s).	editor(s)
equiv	equivalent(s)
Et	ethyl
g	gram(s)
GPC	gel permeation chromatography
h	hour(s)
HRMS	high-resolution mass spectrum
Hz	hertz (s^{-1})
i	iso
i.e.	that is
IR	infrared (spectrum)
J	coupling constant (in NMR)
LDA	lithium diisopropylamide
m	multiplet (spectral), meter(s), milli
M	molar (1 M = 1•mol dm^{-3})
Me	methyl
mg	milligram(s)
MHz	megahertz
min	minute(s)
mL	milliliter(s)
mm	millimeter(s)
mmol	millimole
Ms	methanesulfonyl
n	normal
Nf	1,1,2,2,3,3,4,4,4-nonafluoro -1-butanesulfonyl
NMR	nuclear magnetic resonance
o	ortho
p	para
PCC	pyridinium chlorochromate
pp.	page(s)
Ph	phenyl
ppm	parts per million (in NMR)
Pr	propyl
q	quartet (spectral)
quant.	quantitative
ref(s)	reference(s)
rt	room temperature
s	singlet (spectral)
s	secondary
t	triplet (spectral)
t	tertiary
TBAF	tetrabutylammonium fluoride
TES	triethylsilyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
THP	2-tetrahydropyranyl
TLC	thin-layer chromatography
TMS	trimethylsilyl
Ts	*p*-toluenesulfonyl
TS	transition state
UV	ultraviolet
vide infra	see below
Vol.	volume

Instrumentation and Materials

^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra were taken on a Varian UNITY INOVA 500 spectrometer unless otherwise noted. Chemical shifts (δ) are in parts per million relative to chloroform at 7.26 ppm for ^{1}H and at 77.0 ppm for ^{13}C or benzene at 7.16 ppm for ^{1}H and at 128.0 ppm for ^{13}C. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck silica gel 60F_{254}. Silica gel (Wakogel 200 mesh) was used for column chromatography. Gel permeation chromatography (GPC) was performed by LC-908 (Japan Analytical Industry Ltd., two in-line JAIGEL-2H, toluene, 7.8 mL/min, UV and RI detectors). Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. 1,2,3,4,5-Pentamethyl-1,3-cyclopentadiene was purchased from Kanto Chemical Co., and stored under argon.

Chapter 1

Nucleophilic Addition of Lithium Pentamethylcyclopentadienide to Carbonyl Compounds and Carbon–Carbon Bond Cleavage of the Adducts Yielding the Parent Carbonyl Compounds

Lithium pentamethylcyclopentadienide (C_5Me_5Li, Cp*Li) reacted with aromatic aldehyde to provide the corresponding carbinol in excellent yield. The carbinol returns to the parent aldehyde and pentamethylcyclopentadiene upon exposure to acid or due to heating. Chlorodimethylaluminum is essential as an additive to attain the nucleophilic addition of Cp*Li to aliphatic aldehyde. The carbinol derived from aliphatic aldehyde returns to the parent aldehyde and pentamethylcyclopentadiene by the action of a catalytic amount of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ). The reversible addition/elimination of the Cp* group can represent a protection of aldehyde. Mechanistic details of the carbon–carbon bond cleavage are also disclosed.

Introduction

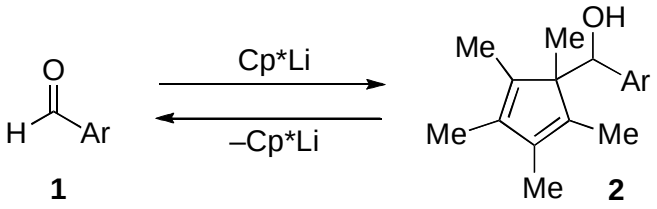
Pentamethylcyclopentadienide ($Me_5C_5^-$, Cp^{*-}) is an extremely important ligand in transition metal chemistry because of its unique structure and electronic property.[1,2] Cp^{*-} serves as a ligand of transition metal catalysts in organic synthesis. However, there are few reports to use Cp^{*-} by itself as a reagent in organic synthesis.[3] The author has been exploring the utility of Cp^{*-} as a reagent in organic synthesis,[4] and here he reports the full details of reversible addition/elimination of the Cp* group to carbonyl, which can represent a protection of a carbonyl group.

Results and Discussion

Addition of Cp^{*-} to Aromatic Aldehydes and its Reverse Process

Treatment of *p*-bromobenzaldehyde (**1a**, 2.0 mmol) with Cp*Li (2.4 mmol, derived from butyllithium and pentamethylcyclopentadiene, Cp*H) in THF at –20 ˚C for 1 h provided the corresponding adduct **2a** in 95% isolated yield (Table 1, entry 1, from **1** to **2**).[5] Reactions at higher temperatures such as 0 ˚C resulted in the concurrence of a side reaction, that is, Meerwein–Ponndrof–Verley reduction/Oppenauer oxidation, to yield *p*-bromobenzyl alcohol and *p*-$BrC_6H_4C(=O)Cp^*$. Use of methylmagnesium bromide instead of butyllithium also enhanced the reduction/oxidation side reaction. The attempted nucleophilic addition reaction led to no or little conversion under Cs_2CO_3/DMSO, $KN(SiMe_3)_2$/THF, or $NaN(SiMe_3)_2$/THF deprotonation conditions. Replacement of Cp*Li with lithium cyclopentadienide (CpLi) led to the formation of the corresponding fulvene by facile dehydration.[6]

Table 1. Formally Reversible Addition of Cp*Li to Aromatic Aldehydes



1 **2**

entry	Ar	from **1** to **2**[a] /%	from **2** to **1**[b] /%
1	*p*-BrC_6H_4 (**a**)	95	92
2	2-Naphthyl (**b**)	88	87
3	*p*-$PhC(=O)C_6H_4$ (**c**)	85	87
4	*p*-$MeOC(=O)C_6H_4$ (**d**)	87	91
5	*p*-NCC_6H_4 (**e**)	95	79
6	*p*-*n*-$BuOC_6H_4$ (**f**)	98	87
7	*p*-*i*-$PrC(=O)C_6H_4$ (**g**)	84	93
8	*o*-$MeOC_6H_4$ (**h**)	97	69

[a] Conditions: 1.2 equiv Cp*Li, THF, –20 ˚C, 1 h; then quenching with water.

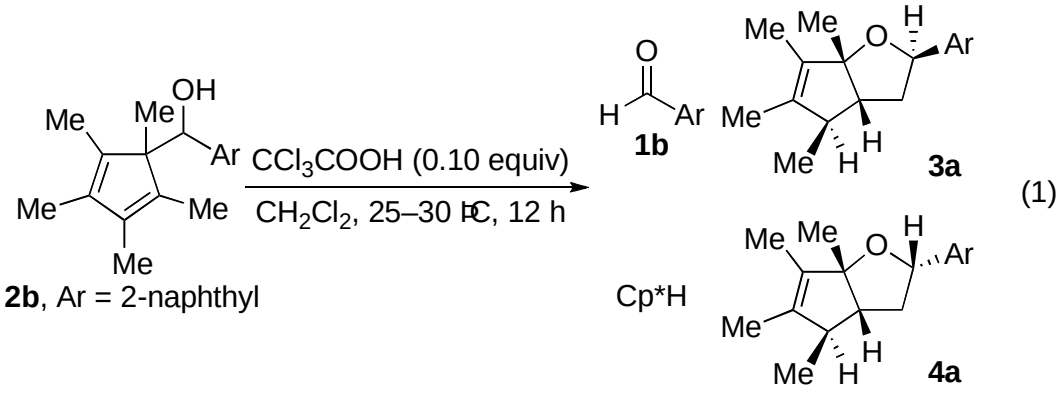
[b] Conditions: 10 mol% trichloroacetic acid, dichloromethane, 25–30 ˚C, 0.25–1.5 h.

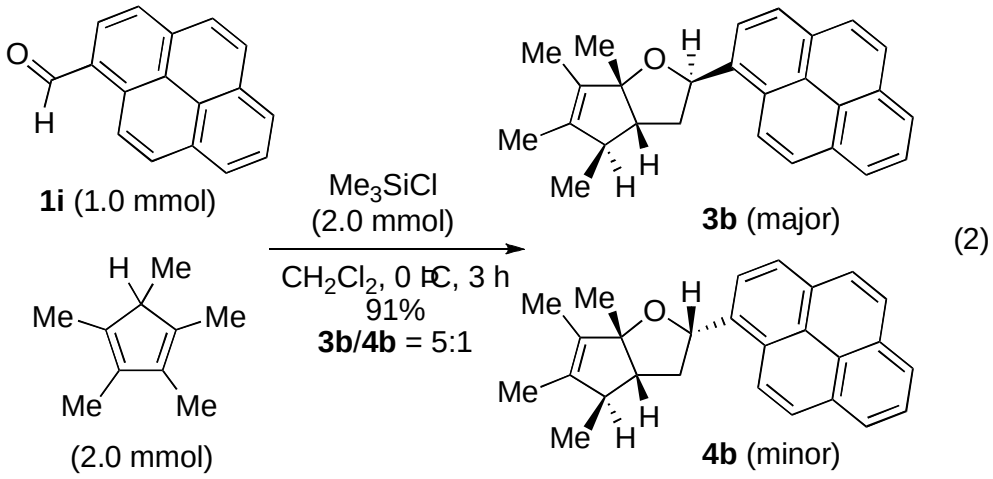
A variety of aromatic aldehydes were subjected to the nucleophilic addition of Cp*Li (Table 1, from **1** to **2**). The reaction was so chemoselective that keto (entries 3 and 7), ester (entry 4), and cyano (entry 5) moieties survived during the reaction. Sterically demanding *ortho*-substitution did not interfere with the reaction (entry 8). In contrast to the reactions with **1c** and **1g**, enolization of *p*-formylacetophenone was inevitable, furnishing the expected adduct in less than 30% yield.

Carbinols **2** were sensitive to acids. Specifically, acid-induced carbon–carbon bond cleavage took place to afford the parent aldehydes and Cp*H.[7,8] Carbinol **2a** was exposed to 10 mol% of trichloroacetic acid in dichloromethane at 25–30 ˚C for 1.5 h to provide **1a** in 92% isolated yield (entry 1, from **2** to **1**). It is worth noting that quantitative recovery of Cp*H upon

the cleavage is advantageous since Cp*H is expensive. Other acids such as trifluoroacetic acid, camphorsulfonic acid monohydrate, *p*-toluenesulfonic acid monohydrate also promoted the carbon–carbon bond cleavage under the otherwise same reaction conditions, although the yields of **1a** were lower by *ca*. 20% because of several unidentified byproducts (vide infra). Acetic acid is too weak to cleave the carbon–carbon bond at a satisfactory rate. Silica gel in dichloromethane did not work at all. In polar coordinating solvents such as THF and methanol, acid-catalyzed cleavage was not observed. Under the standard reaction conditions, all the carbinols **2** returned to the parent aldehydes (Table 1, from **2** to **1**).

The progress of the acid-induced cleavage should be monitored by thin layer chromatography. When the reaction was performed for an unnecessarily long time or with a too strong acid, the reactions yielded more complex mixtures. For instance, the reaction of **2b** with trichloroacetic acid overnight gave not only **1b** and Cp*H but also **3a** and **4a** (eq. 1, yields undetermined). The formations of **3a** and **4a** are unusual, and the exact structures of **3a** and **4a** were not determined even with the aid of two-dimensional NMR technique. However, it was proved that the treatment of **1b** with Cp*H in the presence of trichloroacetic acid provided a mixture of **3a** and **4a**. Moreover, the use of chlorotrimethylsilane instead of trichloroacetic acid improved the yield of **3a** and **4a**. Then, the aldehyde **1i** was chosen in place of **1b** and treated with Cp*H in the presence of chlorotrimethylsilane to give more suitable compounds **3b** and **4b**, the analogues of **3a** and **4a** for X-ray crystallographic analysis. Luckily the structures of **3b** and **4b** were fully determined by X-ray crystallographic analysis (Figure 1)[9] as well as by ^{1}H NMR, ^{13}C NMR, DEPT, and COSY spectra. The products **3b** and **4b** are epimers, with respect to the location of the pyrenyl ring. Other acids such as trichloroacetic acid also mediated the same transformation, while the yields of **3b** and **4b** were low. The mechanism for the formation of **3b** and **4b** is unclear.





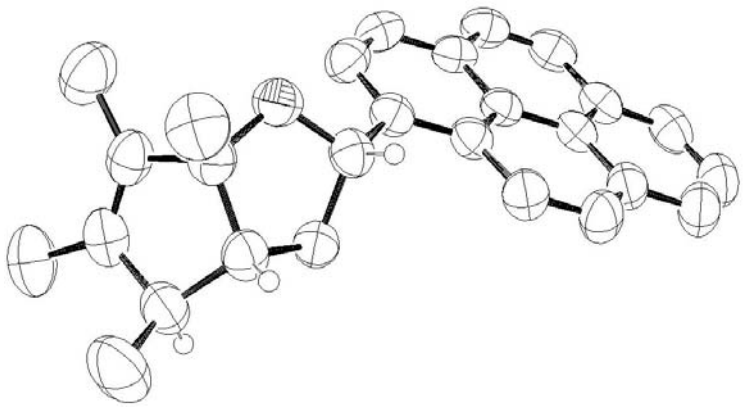
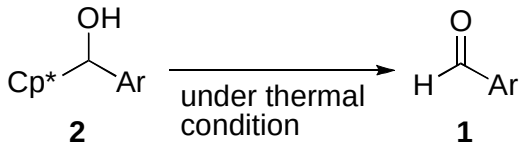


Figure 1. ORTEP drawing of **4b**. Thermal ellipsoids are 50% probability level. Three hydrogen atoms are shown for convenience.

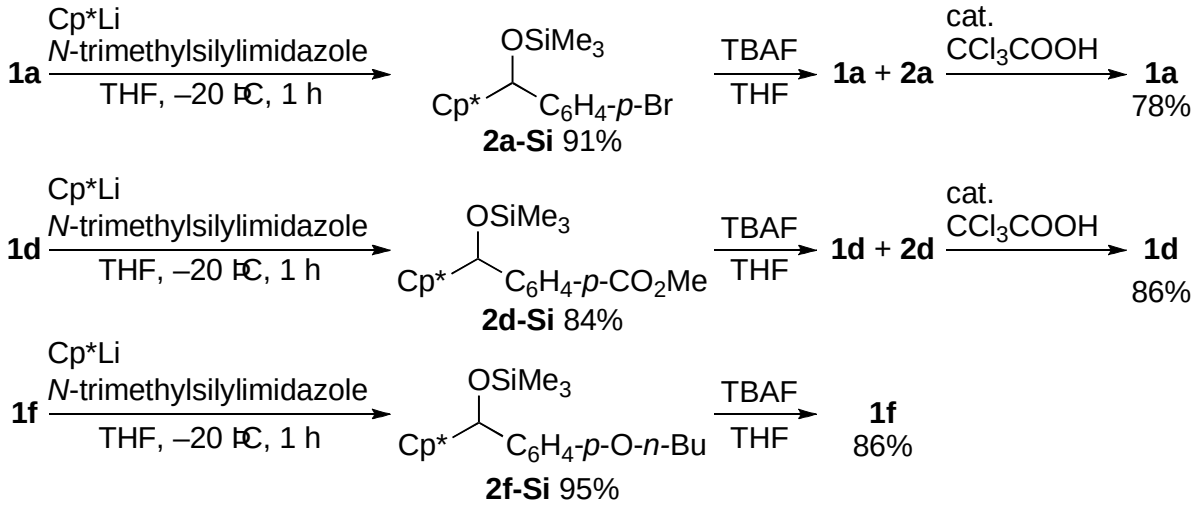
A similar carbon–carbon bond cleavage was observed in the absence of acid, which can avoid the careful monitoring. Boiling **2a** and **2e** in toluene furnished aldehydes **1a** and **1e** in 88% and 93% yields, respectively (eq. 3). Electron-rich carbinol **2f** required a higher temperature to return efficiently to **1f** in boiling xylene. Complete conversion of **2f** in refluxing toluene took more than 20 h, albeit the yield was quantitative.



1a (88%, 0.5 h, toluene, reflux)
1e (93%, 3 h, toluene, reflux)
1f (97%, 3 h, xylene, reflux) (3)

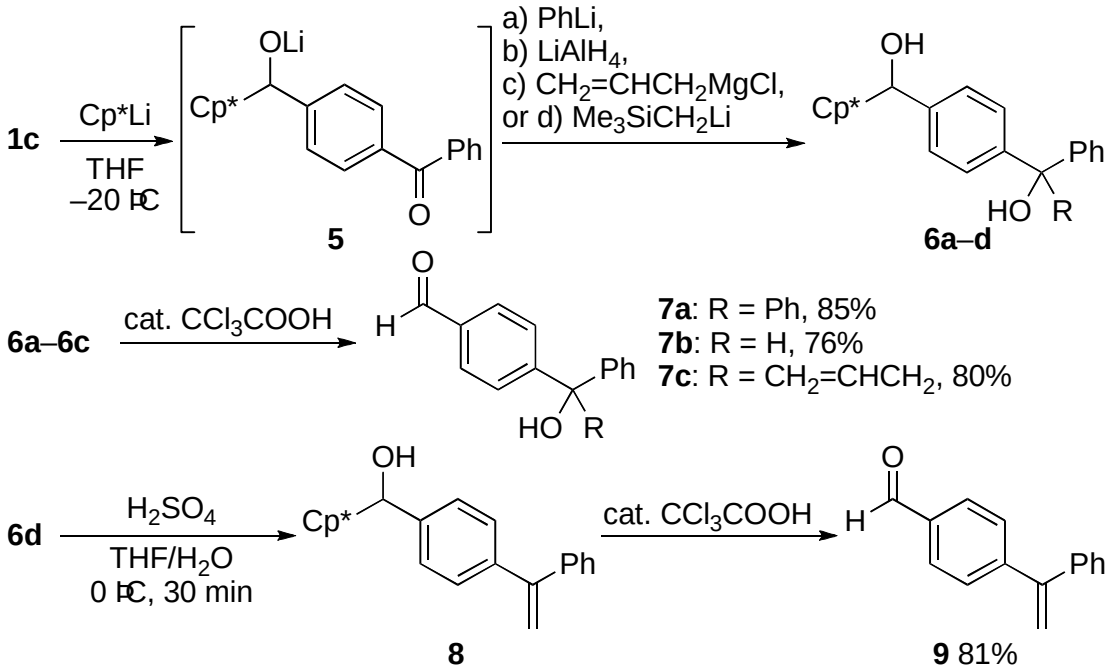
The lithium alkoxides of **2** can be trapped with *N*-trimethylsilylimidazole to provide the corresponding trimethylsilyl ethers (Scheme 1). *N*-Trimethylsilylimidazole is the best reagent for the trapping. Chlorotrimethylsilane, trimethylsilyl triflate, and other *N*-silylimidazoles were less effective. Interestingly, the silyl ethers **2-Si** could return to **1** with the aid of tetrabutylammonium fluoride. The generation of **1** did not go to completion in some cases. However, treatment of the crude mixture of **1** and **2** with trichloroacetic acid afforded **1** in reasonable overall yield.

Scheme 1.



The utility of the Cp* group as a protective group is outlined in Scheme 2. After Cp* had masked the aldehyde moiety of **1c** *in situ*, the keto group was subjected to nucleophilic addition reaction with phenyllithium to afford diol **6a**. The crude oil was exposed to the acidic conditions to produce hydroxy aldehyde **7a** in 85% overall yield. Chemoselective reduction and allylation provided **7b** and **7c**, respectively.[10,11] Attempted Wittig reaction of **5** with CH_2=PPh_3 failed, and the methylenation of the aldehyde moiety that must be masked was partly observed. Alternatively, addition of trimethylsilylmethyllithium to **5** followed by acid-catalyzed olefination in aqueous THF yielded carbinol **8**. Treatment of **8** under the deprotection conditions afforded **9** in 81% overall yield. All the procedures proceeded so cleanly that no purification of the intermediates such as **6** and **8** was necessary.

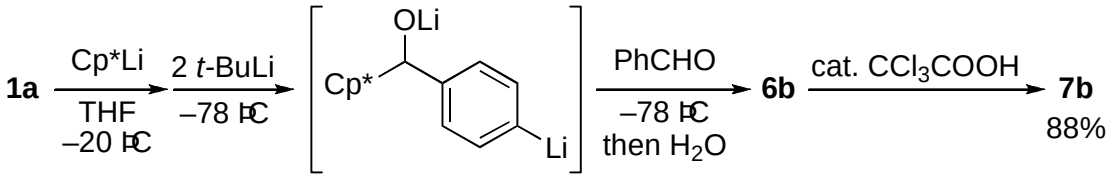
Scheme 2.



The protective method allowed for preparation of a formyl-substituted phenyllithium equivalent (Scheme 3). Nucleophilic addition of Cp*Li to **1a** followed by bromine–lithium exchange furnished the corresponding aryllithium. The lithium reagent could be trapped with

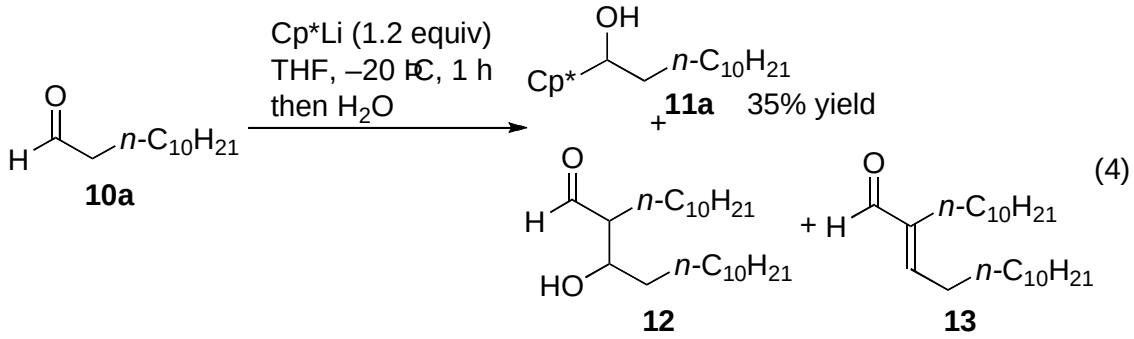
benzaldehyde to yield crude diol **6b**. Subsequent removal of Cp*H afforded **7b** in 88% overall yield.

Scheme 3.



Addition of Cp*⁻ to Aliphatic Aldehyde and Ketone with the Aid of Chlorodimethylaluminum and Its Reverse Process

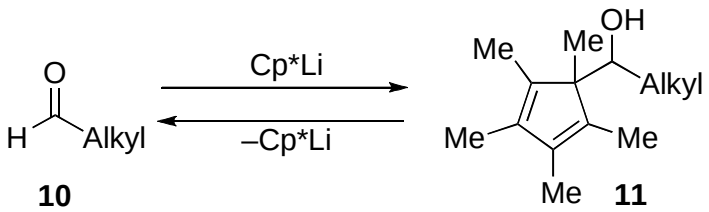
The reaction of Cp*Li with aliphatic aldehyde failed to yield a satisfactory amount of the corresponding adduct. For instance, treatment of dodecanal (**10a**) with Cp*Li afforded the corresponding adduct **11a** in only 35% yield (eq. 4). The byproducts mainly comprised β-hydroxy aldehyde **12** and α,β-unsaturated aldehyde **13**, which means that Cp*Li served as a base to generate the lithium enolate of **10a**. Many additives were thus screened, and the author found that chlorodimethylaluminum promotes the addition of Cp*⁻ to aliphatic aldehydes.



Chlorodimethylaluminum (6.0 mmol) was added to a suspension of Cp*Li (6.0 mmol) in THF at –20 ˚C. Aldehyde **10a** (5.0 mmol) was then added, and the mixture was stirred at –20 ˚C for 1 h. Extractive workup followed by silica gel column purification provided alcohol **11a**

in 92% yield (Table 2, entry 1, from **10** to **11**). Trace amounts of **12** and **13** were detected in the crude oil. The role of chlorodimethylaluminum is unclear. No visible or spectroscopic changes of significance were observed. Chlorodimethylaluminum can activate the carbonyl group as a Lewis acid. Alternatively, Cp*$AlMe_2$ reagent may be formed *via* transmetalation and can effect the selective nucleophilic attack. Other Lewis acids including chlorotrimethylsilane, triethylaluminum, and magnesium dibromide were much less effective than chlorodimethylaluminum. Titanium tetraisopropoxide similarly assisted the addition reaction (81% yield).

Table 2. Formally Reversible Addition of Cp*Li to Aliphatic Aldehydes

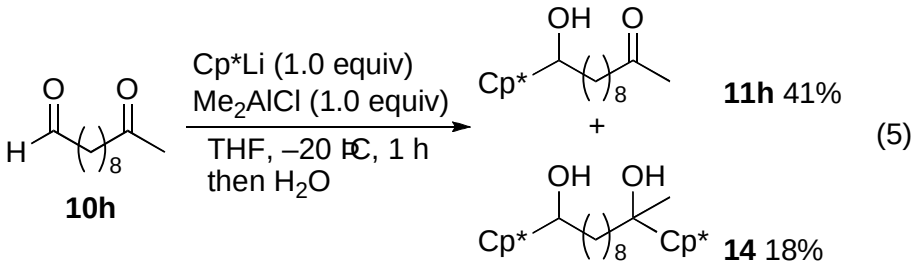


10 **11**

entry	Alkyl	from **10** to **11**[a] /%	from **11** to **10**[b] /%
1	$CH_3(CH_2)_{10}$ (**a**)	92	92 (12 h)
2	$PhCH_2CH_2$ (**b**)	94	80 (12 h)
3[c]	*c*-C_6H_{11} (**c**)	97	82 (24 h)[d]
4	*t*-C_4H_9 (**d**)	<10	–
5	$NC(CH_2)_5$ (**e**)	89	75 (24 h)
6	$Cl(CH_2)_9$ (**f**)	93	95 (12 h)
7	$CH_3OC(=O)(CH_2)_4$ (**g**)	82	81 (36 h)

[a] Conditions: 1.2 equiv Cp*Li, 1.2 equiv Me_2AlCl, THF, –20 ˚C, 1 h; then quenching with water. [b] Conditions: 1 mol% DDQ, toluene, reflux. The reaction time of each run is in parentheses. [c] To complete the reaction, 1.5 equiv of Cp*Li and Me_2AlCl were used. [d] Isolated as 1-cyclohexylpentanol after treatment of the crude oil with butyllithium because cyclohexanecarbaldehyde is volatile.

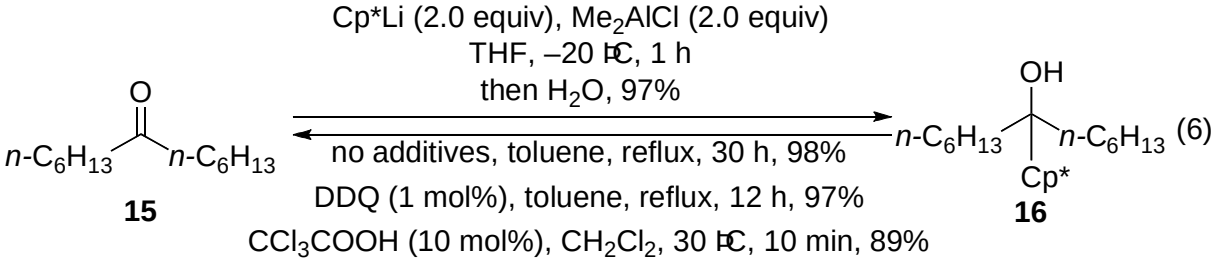
The nucleophilic addition is applicable to a wide range of aliphatic aldehydes (Table 1, from **10** to **11**). Whereas the reaction of cyclohexanecarbaldehyde (**10c**) cleanly provided **11c**, sterically congested pivalaldehyde (**10d**) resisted the reaction. The reaction was chemoselective enough to leave cyano, chloro, and ester moieties untouched (entries 5–7). The reactions with catalytic amounts of chlorodimethylaluminum did not go to completion and gave rise to *ca.* 80% conversion. Unfortunately, the reaction with keto aldehyde **10h** exhibited unsatisfactory chemoselectivity (eq. 5).



(5)

Removal of the Cp* group of **11**, which corresponds to regeneration of **10**, can represent a protective method of aliphatic aldehydes. Contrary to the instability of aromatic carbinols **2** under the acidic or thermal conditions, carbinols **11** were stable toward acids or at high temperature. By extensive screening of reaction conditions, 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), proved to induce smooth carbon–carbon bond cleavage to produce the parent aldehyde **10** and Cp*H. Treatment of **11a** with 1 mol% of DDQ in boiling toluene for 12 h furnished **10a** in 92% isolated yield (entry 1, from **11** to **10**), with quantitative generation of Cp*H. With the aid of DDQ, all the carbinols **11** returned to the original aldehydes (Table 1, from **11** to **10**). Carbinols **11e** and **11g** with polar cyano and ester moieties were transformed more slowly to **10e** and **10g**, respectively. The bulkier cyclohexyl group of **11c** also retarded the reaction. Other organic oxidants such as chloranil, 2,3-dichlorobenzoquinone, trityl tetrafluoroborate ($Ph_3C^+BF_4^-$) also facilitated the removal albeit the efficiency was much lower.

Chlorodimethylaluminum also promoted the addition onto dihexyl ketone (**15**) (eq. 6). Without the additive, enolization of **15** predominated and none of **16** was obtained. Interestingly, boiling **16** in toluene for 30 h yielded **15** and Cp*H quantitatively. It is worth noting that DDQ accelerated the transformation (reflux, 12 h). A catalytic amount of trichloroacetic acid also effected the degradation of **16** into **15** and Cp*H.

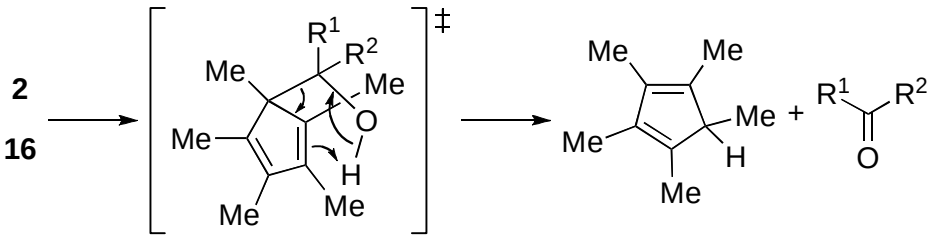


(6)

Mechanisms for the carbon–carbon bond cleavage

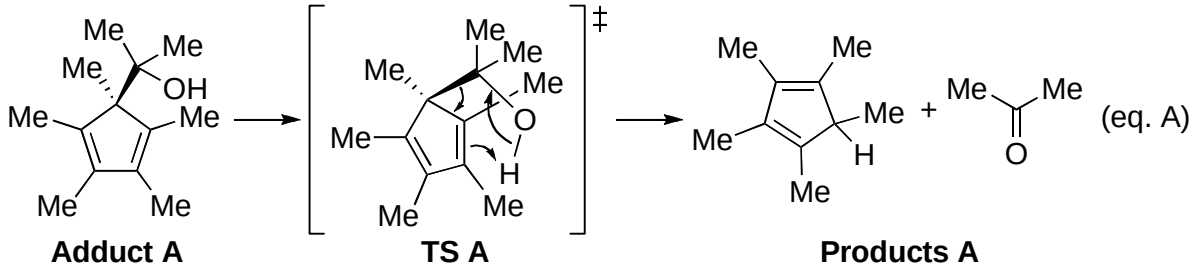
A concerted retro-carbonyl-ene mechanism can rationalize the fragmentation reaction under the thermal cleavage conditions (Scheme 4).[12] Generally, thermal retro-carbonyl-ene reactions require higher temperature, most of which were performed in a gas phase.[12e] The reaction temperatures used herein are low as being temperatures for retro-carbonyl-ene reactions.

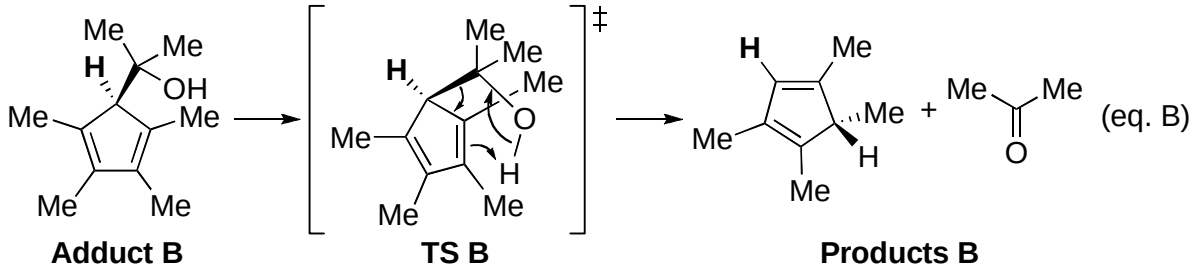
Scheme 4.

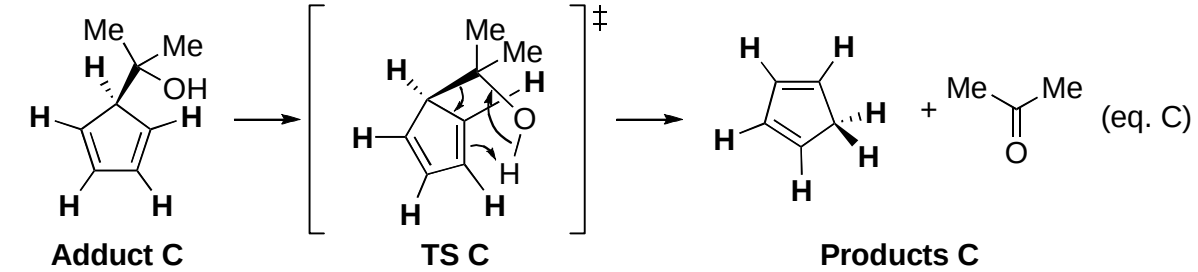


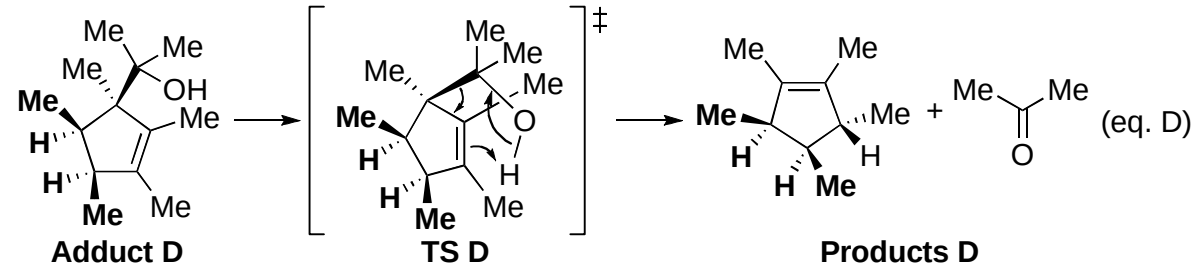
To clarify the origin of the facile retro-carbonyl-ene process, the author set up five simplified models, equations A–E, and performed ab initio calculations. The energy profile of the model reactions is shown in Figure 2. The activation barrier of the retro-carbonyl-ene

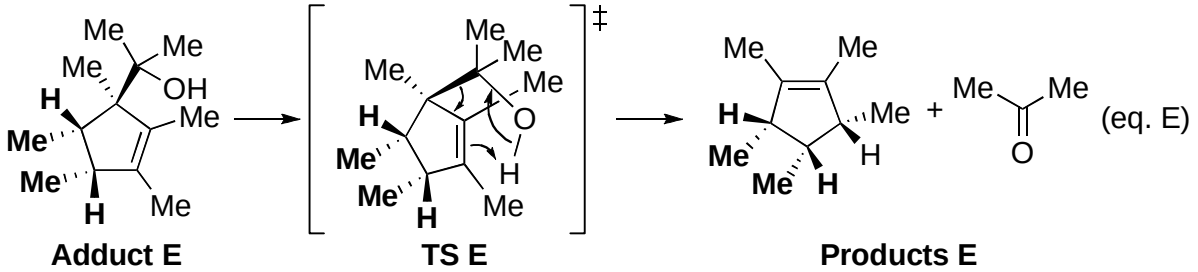
reaction from **Adduct A** to **Products A** was calculated to be 29.25 kcal/mol. The higher barrier of 33.18 kcal/mol in eq. B suggests that the methyl group at the 1 position of Cp* plays an important role to enhance the carbon–carbon bond cleavage. The removal of the cyclopentadienyl group, without any methyl groups on the cyclopentadiene ring, should go over the higher barrier (35.97 kcal/mol) from **Adduct C** to **Products C** (eq. C). The steric hindrance of the Cp* group thus contributes to the facile retro-carbonyl-ene reaction. In addition, the conjugated diene system of Cp* proved to be much more important than the steric factor, by comparison of the activation barriers of eq. A, D, and E. The activation barriers of eq. D and E, wherein pentamethylcyclopentenes liberate, are calculated to be higher than that of eq. A by *ca*. 10 kcal/mol. The characteristic features of the Cp* group, i.e., its steric bulkiness and conjugated diene system, allows for the retro-carbonyl-ene reaction at a low temperature. It is worth noting that the activation barrier of the retro-carbonyl-ene reaction of 2-methyl-4-penten-2-ol was calculated to be 35.40 kcal/mol at the B3LYP/6-311+G**//RHF/6-311+G** levels of theory.[13]


Adduct A
TS A
Products A
(eq. A)


Adduct B
TS B
Products B
(eq. B)


Adduct C
TS C
Products C
(eq. C)


Adduct D
TS D
Products D
(eq. D)


Adduct E
TS E
Products E
(eq. E)

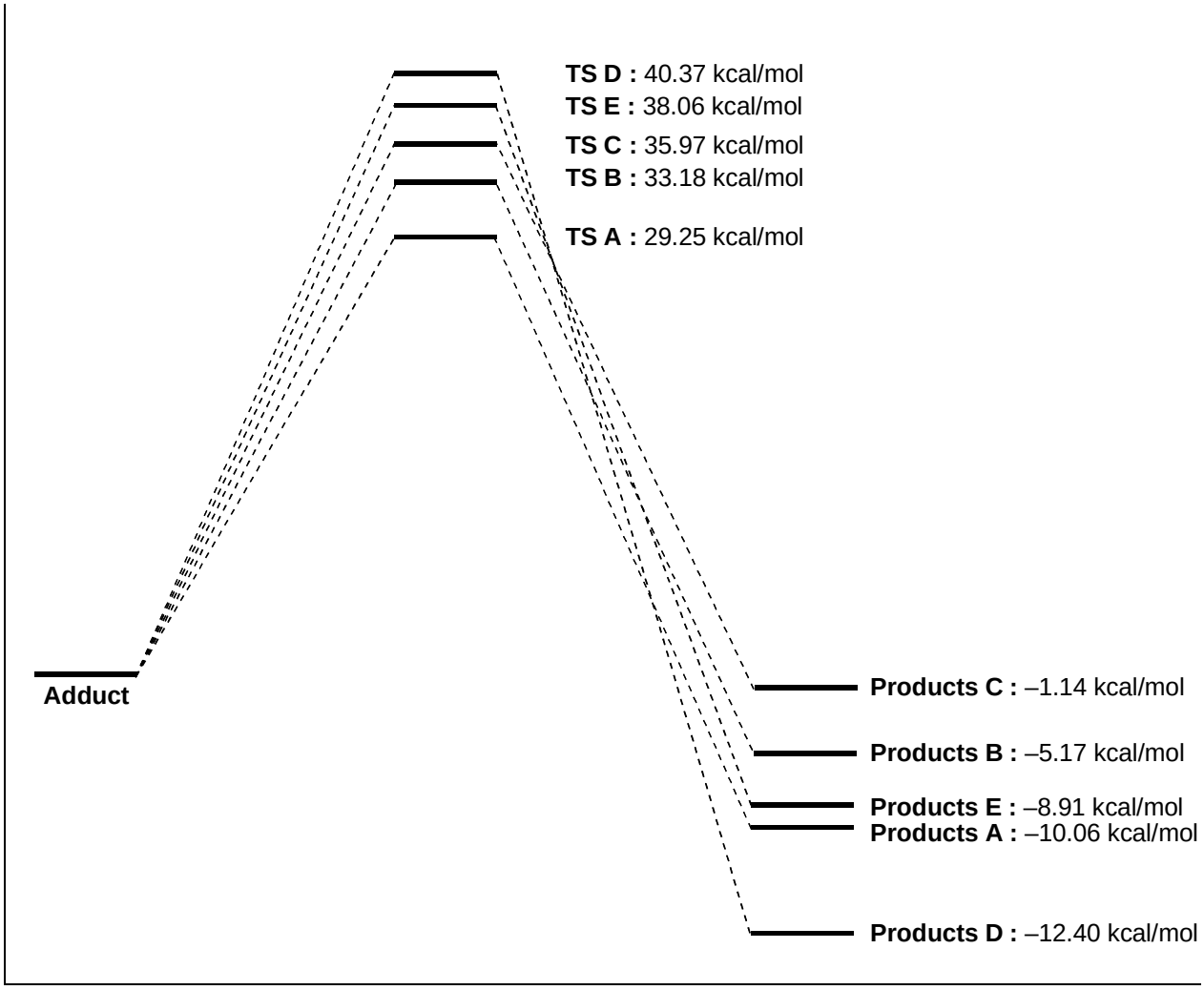
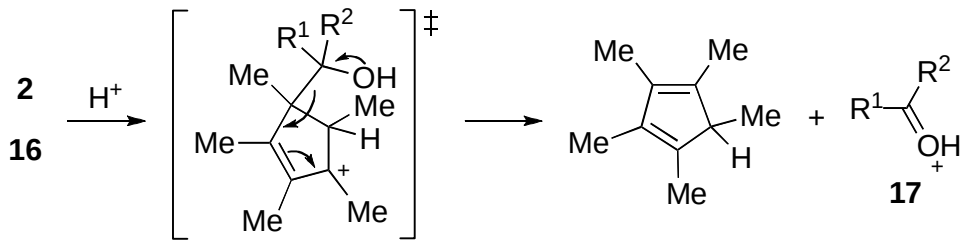


Figure 2. Calculated energy profile for eq. A–E at the B3LYP/6-311+G**//RHF/6-311+G** levels of theory.

Under the acid-catalyzed conditions, protonation at the Cp* group would facilitate the carbon–carbon bond cleavage (Scheme 5). The Cp* group would be more easily protonated than the hydroxy group.[14] As described, the acid-catalyzed cleavage did not take place in a coordinating solvent. A coordinating solvent would interfere with the protonation of the Cp* group. Solvents of less coordinating nature such as dichloromethane facilitated the protonation. The protonation would promote release of the steric hindrance and recovery of a stabilized conjugated diene and result in carbon–carbon bond cleavage to form Cp*H and oxonium cation

17.

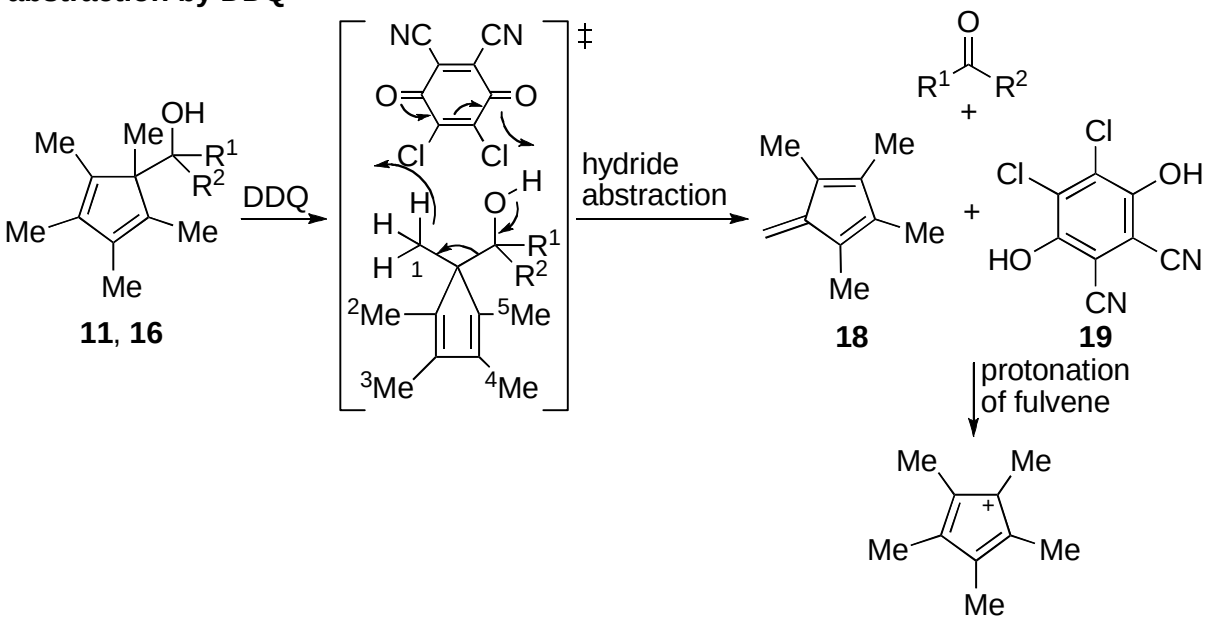
Scheme 5.



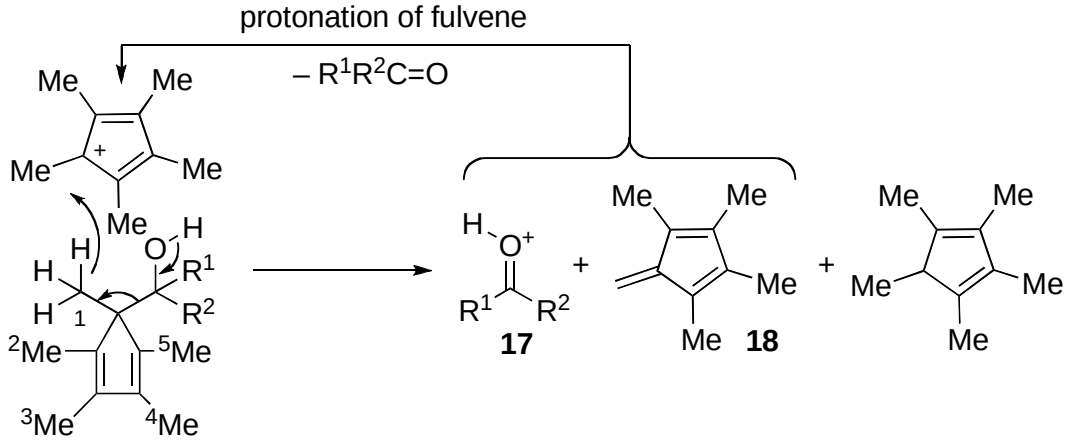
While the mechanism of the DDQ-promoted cleavage is not clear, the author is tempted to propose two possible mechanisms (Scheme 6). One mechanism begins with hydride abstraction by DDQ, a strong hydride acceptor.[15] DDQ would abstract the hydride at the 1-methyl group of the Cp* group,[16] which generates the original carbonyl compound, tetramethylfulvene (**18**), and **19**. Protonation of **18** with **19** would yield unstable pentamethylcyclopentadienyl cation (Cp*$^+$).[17] The cyclic 4π-electronic cation Cp*$^+$ would be a hydride acceptor efficient enough to abstract hydride from Cp*R^{1}R^{2}COH to produce oxonium cation **17**, **18**, and Cp*H. Protonation of the fulvene **18** with the oxonium cation **17** again generates Cp*$^+$ to complete the catalytic cycle. An alternative scenario involves single electron transfer.[18] Single electron transfer from Cp*R^{1}R^{2}COH to DDQ generates radical anion **20** and radical cation **21**. The cation **21** undergoes fragmentation into pentamethylcyclopentadienyl radical (Cp*•) and the original carbonyl compound. Cp*• would be oxidized by **22** to form Cp*$^+$. The cation Cp*$^+$ takes part in the same catalytic cycle in the hydride abstraction mechanism. It is noteworthy that no deuterium incorporation was observed in the cleavage reaction in toluene-d_8, which eliminates the possibility of hydrogen abstraction of the possible radical intermediates from solvent.

Scheme 6.

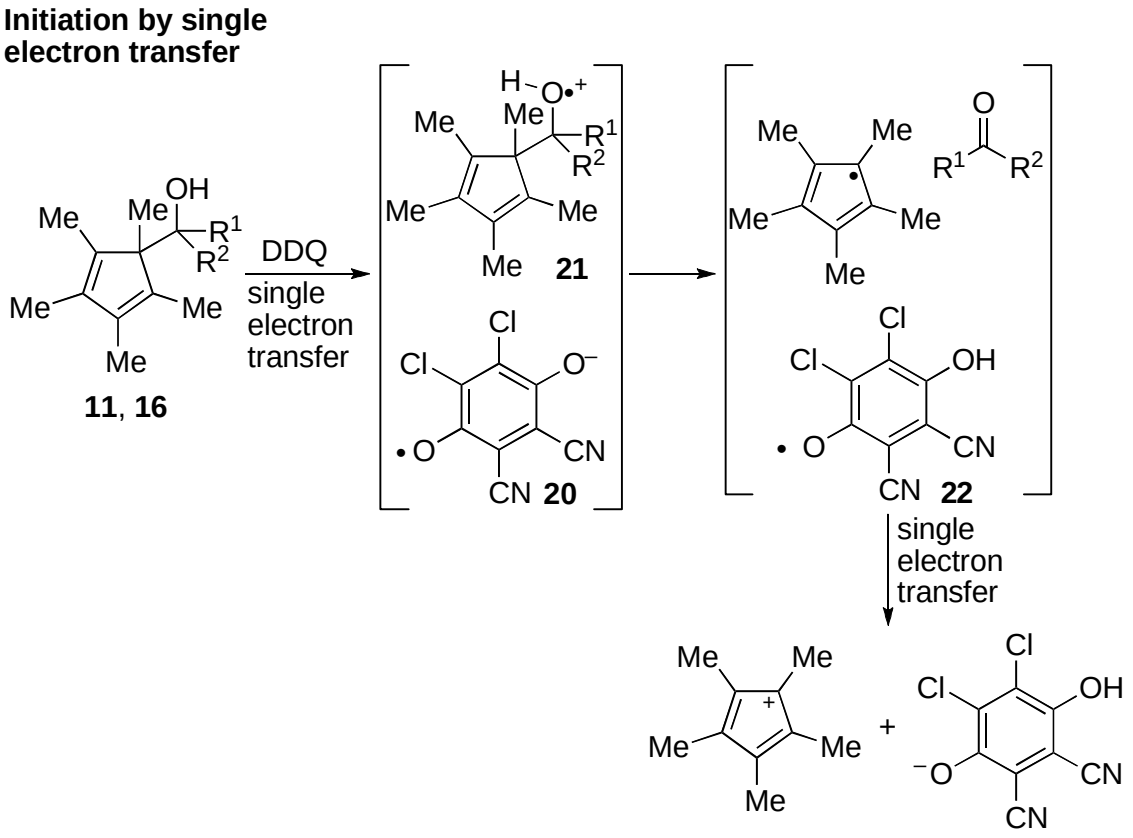
Initiation by hydride abstraction by DDQ



Productive propagation step



Scheme 6. (Continued)



The hydroxy group of **11** plays a key role in the carbon–carbon bond cleavage process. Additional polar groups such as cyano and ester groups in **11e** and **11g** would prevent the weak interaction between the hydroxy group and electron deficient species such as DDQ and Cp^{*+}. The bulkier cyclohexyl group of **11c** hampered the access of the electron deficient species to the hydroxy group of **11c**. Namely, rate-determining hydride abstraction or single electron transfer would be retarded. It is worth noting that the silyl ether of **11b** completely resisted the cleavage upon treatment with DDQ in boiling toluene.

Conclusion

Pentamethylcyclopentadienide has now participated in organic synthesis as a new "reagent". The protection of an aldehyde moiety with Cp* emerges by utilizing the facile cleavage of the Cp^{*}–CR^1R^2OH bond. The cleavage is due to the unique nature of Cp* group.

Experimental Section

Theoretical Calculations

All the calculations were performed by using Spartan '04.[19] All the structures were optimized at the HF/6-311+G** level of theory. Single point calculations of the total energies were performed at the B3LYP/6-311+G** at the HF/6-311+G** optimized geometries. The transition states obtained gave proper single imaginary frequencies.

General Procedure for Nucleophilic Addition of Cp^*Li to Aromatic Aldehydes (Table 1)

A solution of butyllithium in hexane (1.6 M, 1.57 mL, 2.4 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.42 mL, 2.6 mmol) in THF (20 mL) at –78 ˚C. The mixture was stirred for 30 min at room temperature to provide a white suspension of lithium pentamethylcyclopentadienide. To the resulting mixture, a solution of *p*-bromobenzaldehyde (**1a**, 370 mg, 2.0 mmol) in THF (3.0 mmol) was added at –20 ˚C, and the reaction mixture was stirred for 1 h at –20 ˚C. After quenching the reaction with water, the mixture was extracted with hexane/ethyl acetate (10:1, 20 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification by chromatography on silica gel afforded **2a** (609.1 mg, 1.90 mmol) in 95% yield.

Acid-Induced Cleavage Reaction (Table 1)

A solution of trichloroacetic acid in dichloromethane (0.1 M, 0.50 mL, 0.05 mmol) was added to a solution of **2a** (160.4 mg, 0.50 mmol) in dichloromethane (3.0 mL) at room temperature. The mixture was stirred for 90 min at 28 ˚C. After quenching the reaction with saturated aqueous $NaHCO_3$, the mixture was extracted with hexane/ethyl acetate (10:1, 20 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Silica gel column purification provided *p*-bromobenzaldehyde (**1a**, 84.8 mg, 0.458 mmol) in 92% yield.

Acid-Mediated Coupling of Pyrenecarbaldehyde with Cp*H (eq. 2)

A mixture of 1-pyrenecarbaldehyde (**1i**, 230 mg, 1.0 mmol) and Cp*H (0.31 mL, 2.0 mmol) was dissolved in dichloromethane (1.0 mL). Chlorotrimethylsilane (0.26 mL, 2.0 mmol) was added dropwise at 0 ˚C. After the mixture was stirred for 4 h at 0 ˚C, the reaction was quenched with saturated aqueous $NaHCO_3$. Work-up followed by silica gel column purification provided **3b** and **4b** in 91% combined yield (330 mg, 0.91 mmol) in a ratio of 5:1.

Thermal Cleavage Reaction (eq. 3)

Carbinol **2a** (643.7 mg, 2.0 mmol) was dissolved in toluene (10 mL). After the solution was stirred at 110 ˚C for 0.5 h, the solvent was removed under reduced pressure. Purification of the residue by chromatography on silica gel gave *p*-bromobenzaldehyde (**1a**, 324.1 mg, 1.75 mmol) in 88% yield.

Synthesis of 2-Si (Scheme 1)

Butyllithium in hexane (1.6 M, 7.4 mL, 12 mmol) was added dropwise to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (2.0 mL, 13 mmol) in THF (100 mL) at –20 ˚C. The resulting suspension was stirred for 30 min. A solution of *p*-bromobenzaldehyde (1.85 g, 10 mmol) in THF (10 mL) was added to the suspension. The reaction mixture was stirred at –20 ˚C for 1 h. *N*-Trimethylsilylimidazole (1.9 mL, 13 mmol) was then added at –20 ˚C, and the resulting mixture was stirred for 1 h at the same temperature. After the reaction was terminated by an addition of water, the organic layer was extracted with ethyl acetate. The combined organic parts were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was purified by column chromatography (Wakogel C-200, pretreated with triethylamine in hexane and eluted with hexane) to afford **2a-Si** (3.60 g, 9.1 mmol, 91 %).

Regeneration of 1f from 2f-Si

A solution of tetrabutylammonium fluoride in THF (1.0 M, 0.60 mL, 0.60 mmol) was

added to a solution of **2f-Si** (193 mg, 0.50 mmol) in THF (3.3 mL) at 0 ˚C. The resulting solution was stirred for 1 h at room temperature. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. Chromatographic purification on silica gel (Wakogel C-200, hexane/ethyl acetate = 20:1) furnished **1f** (76.5 mg, 0.43 mmol, 86 %).

From 2a-Si to 1a

Tetrabutylammonium fluoride (1.0 M THF solution, 0.60 mL, 0.60 mmol) was added to a solution of **2a-Si** (197 mg, 0.50 mmol) in THF (1.7 mL) at 0 ˚C. The resulting mixture was stirred for 1 h at room temperature. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic parts were washed with brine, dried, and concentrated *in vacuo* to give a crude oil. Trichloroacetic acid in dichloromethane (0.1 M, 0.5 mL, 0.05 mmol) was added to the crude oil in dichloromethane (3.3 mL) at 30 ˚C. After 1 h, the reaction was quenched with saturated aqueous $NaHCO_3$, and the mixture was extracted with ethyl acetate. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Silica gel column chromatography (Wakogel C-200, hexane/ethyl acetate = 20:1) yielded 72.1 mg of **1a** (0.39 mmol, 78 %).

From 2d-Si to 1d

Tetrabutylammonium fluoride (1.0 M THF solution, 0.60 mL, 0.60 mmol) was added to a solution of **2d-Si** (186 mg, 0.50 mmol) in THF (1.7 mL) at 0 ˚C. The resulting mixture was stirred for 1 h at room temperature. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated. Trichloroacetic acid (0.1 M in dichloromethane, 0.5 mL, 0.05 mmol) was added to the crude oil in dichloromethane (3.3 mL) at 30 ˚C and the mixture was stirred for 1 h. Additional trichloroacetic acid in dichloromethane (0.1 M, 0.5 mL, 0.05 mmol)

was added to the reaction mixture, and the reaction mixture was stirred for another 30 min. After being quenched with saturated aqueous $NaHCO_3$, the mixture was extracted with ethyl acetate. Usual workup followed by purification on silica gel (Wakogel C-200, hexane/ethyl acetate = 10:1) provided **1d** (70.7 mg, 0.43 mmol, 86 %).

Synthesis of 7a from 1c (Scheme 2)

Butyllithium (1.6 M hexane solution, 0.39 mL, 0.60 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.11 mL, 0.65 mmol) in THF (5 mL) at –78 ˚C under argon. By removing a dry ice/acetone bath, the resulting mixture was allowed to warm to room temperature. After being stirred at room temperature for 30 min, the mixture was cooled to –20 ˚C. Keto aldehyde **1c** (105 mg, 0.50 mmol in 1.5 mL of THF) was then added. The mixture was stirred for 1 h at the same temperature. The reaction mixture was then cooled to –78 ˚C. Phenyllithium (0.98 M in cyclohexane/ether, 0.77 mL, 0.75 mmol, Kanto Chemical Co.) was added and the whole mixture was stirred for 20 min. Water (10 mL) was added at –78 ˚C to quench the reaction. Extractive workup afforded a crude oil of **6a**. Trichloroacetic acid in dichloromethane (0.1 M, 0.5 mL, 0.05 mmol) was added to the crude oil in dichloromethane (3 mL) under argon at 25–30 ˚C, and the resulting solution was stirred for 1 h. After being quenched with saturated aqueous $NaHCO_3$, the mixture was extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous sodium sulfate. Evaporation followed by silica gel column purification (Wakogel C-200, hexane/ethyl acetate = 3:1) yielded 123 mg of **7a** (0.427 mmol, 85% overall yield).

Synthesis of 7b from 1c (Scheme 2)

Butyllithium (1.6 M hexane solution, 0.75 mL, 1.2 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.21 mL, 1.3 mmol) in THF (10 mL) at –20 ˚C. After being stirred for 30 min, keto aldehyde **1c** (210 mg, 1.0 mmol in 3.0 mL of THF) was then added. The mixture was stirred for 1 h at the same temperature. The reaction mixture was

then cooled to –78 ˚C. Lithium aluminum hydride (57 mg, 1.5 mmol) was added in one portion. The whole mixture was stirred for 1 h at 0 ˚C. Water (10 mL) was added to quench the reaction. Extractive workup gave a crude oil of **6b**. Trichloroacetic acid in dichloromethane (0.1 M, 1.0 mL, 0.1 mmol) was added to a solution of **6b** in dichloromethane (6.7 mL) under argon at 25–30 ˚C, and the resulting solution was stirred for 1 h. After being quenched with saturated aqueous $NaHCO_3$, the mixture was extracted with ethyl acetate (20 mL × 3). Removal of volatiles followed by silica gel column purification (Wakogel C-200, hexane/ethyl acetate = 2:1) yielded 136 mg of **7b** (0.76 mmol, 76% overall yield).

Synthesis of 7c from 1c (Scheme 2)

After similar treatment of **1c** (0.50 mmol-scale) with Cp^*Li at –20 ˚C, allylmagnesium chloride (0.92 M ethereal solution, 1.1 mL, 1.0 mmol) was added to the reaction flask at –20 ˚C. The whole mixture was stirred for 1 h. Quenching with water (10 mL) followed by extractive workup gave a crude oil of **6c**. Trichloroacetic acid in dichloromethane (0.1 M, 1.0 mL, 0.1 mmol) was added to a solution of **6c** in dichloromethane (5 mL) under argon at 25–30 ˚C, and the resulting solution was stirred for 45 min. After the reaction was quenched with saturated aqueous $NaHCO_3$, extraction, evaporation, and purification on silica gel (Wakogel C-200, hexane/ethyl acetate = 5:1) furnished 101 mg of **7c** (0.402 mmol, 80% overall yield).

Synthesis of 9 from 1c (Scheme 2)

The reaction started from 0.50 mmol of **1c**. Trimethylsilylmethyllithium (0.66 M pentane solution, 1.5 mL, 1.0 mmol) was added at –78 ˚C to **5** prepared by the method described above. The resulting mixture was stirred for 30 min. Quenching with water (10 mL) followed by extraction with ethyl acetate gave **6d**. Under air, 2.0 M aqueous sulfuric acid (1.0 mL) was added to a solution of crude **6d** in THF/H_2O (4.0 mL/1.0 mL) at 0 ˚C. The mixture was stirred for 30 min at the same temperature. After an addition of saturated aqueous $NaHCO_3$, extraction with ethyl acetate and evaporation under reduced pressure afforded crude **8**, clean formation of

which NMR analysis revealed. Trichloroacetic acid in dichloromethane (0.1 M, 0.5 mL, 0.05 mmol) was added to a solution of **8** in dichloromethane (3 mL) under argon at 25–30 ˚C, and the resulting solution was stirred for 30 min. After the reaction was quenched with saturated aqueous $NaHCO_3$, extraction, evaporation, and purification on silica gel (Wakogel C-200, hexane/ethyl acetate = 10:1) furnished 84.3 mg of **9** (0.405 mmol, 81% overall yield).

Synthesis of 7b from 1a (Scheme 3)

Butyllithium (1.6 M hexane solution, 0.75 mL, 1.2 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.21 mL, 1.3 mmol) in THF (10 mL) at –78 ˚C, and the resulting mixture was allowed to warm to room temperature. After being stirred for 30 min, the mixture was cooled to –20 ˚C. Bromo aldehyde **1a** (186 mg, 1.0 mmol in 1.5 mL of THF) was then added and the mixture was stirred for 1 h at the same temperature. The reaction mixture was then cooled to –78 ˚C and *t*-butyllithium in pentane (1.56 M, 1.4 mL, 2.2 mmol) was added. After 40 min, benzaldehyde (0.16 mL, 1.6 mL) was added and the whole mixture was stirred for an additional 40 min at –78 ˚C. Water (10 mL) was added to quench the reaction. Extractive workup gave a crude oil of **6b**. Trichloroacetic acid in dichloromethane (0.1 M, 1.0 mL, 0.1 mmol) was added to a solution of **6b** in dichloromethane (4 mL) under argon at 25–30 ˚C, and the resulting solution was stirred for 30 min. Workup as above followed by silica gel column purification (Wakogel C-200, hexane/ethyl acetate = 2:1) yielded 187 mg of **7b** (0.88 mmol, 88% overall yield).

General Procedure for Nucleophilic Addition of Cp*Li to Aliphatic Aldehydes (Table 2)

A solution of butyllithium in hexane (1.6 M, 3.8 mL, 6.0 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.95 mL, 6.5 mmol) in THF (50 mL) at –20 ˚C. The mixture was stirred for 30 min at the same temperature to provide a white suspension of lithium pentamethylcyclopentadienide. Chlorodimethylaluminum in hexane (1.0 M, 6.0 mL, 6.0 mmol) was added to the resulting mixture, and the reaction mixture was stirred for 30 min at

–20 ˚C. After an addition of dodecanal (**10a**, 1.1 mL, 5.0 mmol), the mixture was stirred for an additional 1 h at –20 ˚C. After being stirred for 1 h, the reaction was quenched with water, and the mixture was extracted with ethyl acetate three times. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane/ethyl acetate = 10:1) to afford **11a** (1.47 g, 92 %).

General Procedure for DDQ-Induced Cleavage (Table 2)

A solution of **11a** (321 mg, 1.0 mmol) in toluene (1.0 mL) was added to a solution of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ, 2 mg, 0.01 mmol) in toluene (19 mL). The mixture was warmed up to 110 ˚C and stirred for 12 h. After the reaction was terminated by an addition of water, the organic layer was extracted with ethyl acetate. The combined organic parts were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude oil obtained was subjected to silica gel column purification (Wakogel C-200, hexane/ethyl acetate = 10:1) to afford **10a** (170 mg, 0.92 mmol, 92 %).

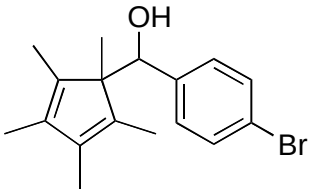
Preparation of 10-Chlorodecanal

To a solution of pyridinium chlorochromate (PCC, 3.9 g, 18 mmol) and silica gel (Silica Gel 60, spherical, neutrality, Nacalai Tesque, 3.9 g) in dichloromethane (60 mL) was added 10-chloro-1-decanol (2.4 mL, 12 mmol). The mixture was stirred for 12 h at room temperature. The resulting mixture was filtered through a pad of Celite 545 and the organic layer was concentrated *in vacuo* to give a crude oil. The crude product was chromatographed on silica gel (Wakogel C-200, hexane/ethyl acetate = 30:1) to afford the title compound (1.7 g, 74 %).

Characterization Data

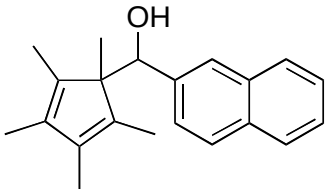
4-[(Hydroxy)(diphenyl)methyl]benzaldehyde (**7a**)[20] and 4-[(hydroxy)(phenyl)methyl] benzaldehyde (**7b**)[21] are found in the literature.

(4-Bromophenyl)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methanol (2a)



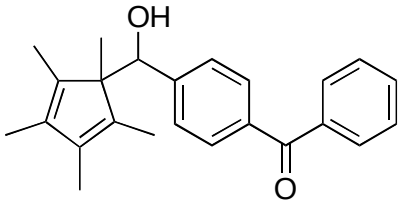
IR (neat) 3458, 2856, 1657, 1591, 1487, 1445, 1379, 1072, 1009, 812, 773, 719, 659, 607 cm^{-1}; ^1H NMR (C_6D_6) δ 1.08 (s, 3H), 1.35–1.42 (m, 1H), 1.43 (s, 3H), 1.49 (s, 3H), 1.52 (s, 3H), 1.95 (s, 3H), 4.31 (d, *J* = 3.0 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (C_6D_6) δ 10.77, 10.82, 11.27, 12.07, 18.09, 61.34, 77.78, 121.02, 128.59, 130.08, 136.40, 136.54, 137.66, 139.28, 140.89. Found: C, 63.58; H, 6.86%. Calcd for $C_{17}H_{21}BrO$: C, 63.56; H, 6.59%.

(2-Naphthyl)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methanol (2b)



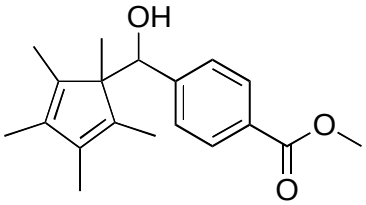
IR (neat) 3444, 3057, 2856, 1654, 1600, 1508, 1444, 1379, 1033, 858, 815, 748, 686, 478 cm^{-1}; ^1H NMR (C_6D_6) δ 1.22 (s, 3H), 1.42 (d, *J* = 1.0 Hz, 3H), 1.50 (d, *J* = 1.0 Hz, 3H), 1.59–1.61 (m, 1H), 1.62 (s, 3H), 2.07 (s, 3H), 4.68 (d, *J* = 3.0 Hz, 1H), 7.20–7.28 (m, 2H), 7.37 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.57 (d, *J* = 8.5 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.67–7.70 (m, 2H); ^{13}C NMR (C_6D_6) δ 10.83, 10.85, 11.50, 12.09, 18.44, 61.50, 78.50, 125.68, 125.81, 125.87, 126.47, 127.86, 127.91, 128.29, 133.21, 133.36, 136.28, 136.40, 138.19, 139.65, 139.68. Found: C, 85.98; H, 8.34%. Calcd for $C_{21}H_{24}O$: C, 86.26; H, 8.27%.

{4-[(Hydroxy)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methyl]phenyl}(phenyl)methanone (2c)



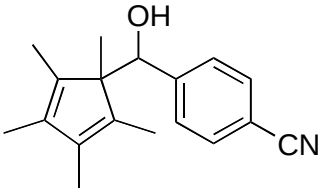
IR (nujol) 3438, 1639, 1604, 1317, 1280, 1147, 1035, 943, 704 cm^{-1}; ^{1}H NMR (C_6D_6) δ 1.14 (s, 3H), 1.47 (s, 3H), 1.51 (s, 3H), 1.58 (s, 3H), 1.40–1.80 (bs, 1H), 2.00 (s, 3H), 4.47 (s, 1H), 7.05–7.20 (m, 5H), 7.68–7.74 (m, 4H); ^{13}C NMR (C_6D_6) δ 10.79, 10.86, 11.34, 12.11, 18.15, 61.26, 78.05, 126.70, 128.26, 128.99, 130.08, 131.83, 136.38, 136.64, 136.70, 137.70, 138.61, 139.45, 146.49, 195.63. Found: C, 82.97; H, 7.58%. Calcd for $C_{24}H_{26}O_2$: C, 83.20; H, 7.56%. m.p. 89–90 ˚C.

Methyl 4-[(hydroxy)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methyl]benzoate (2d)



IR (nujol) 3521, 1706, 1608, 1438, 1282, 1109, 1049, 1018, 763, 711 cm^{-1}; ^{1}H NMR (C_6D_6) δ 1.26 (d, *J* = 4.0 Hz, 3H), 1.35–1.55 (bs, 1H), 1.43 (s, 3H), 1.47 (s, 3H), 1.57 (s, 3H), 1.99 (s, 3H), 3.46 (s, 3H), 4.41–4.45 (m, 1H), 7.15–7.18 (m, 2H), 8.04–8.09 (m, 2H); ^{13}C NMR (C_6D_6) δ 10.73, 10.79, 11.26, 12.12, 18.07, 51.41, 61.18, 78.07, 126.79, 128.42, 129.46, 136.35, 136.61, 137.59, 139.39, 147.09, 166.72. Found: C, 75.82; H, 8.16%. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05%. m.p. 91–92 ˚C.

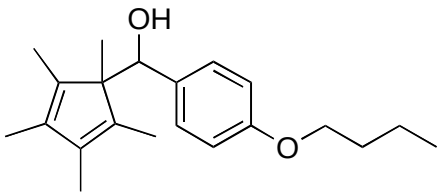
4-[(Hydroxy)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methyl]benzonitrile (2e)



IR (nujol) 3488, 2220, 1606, 1313, 1201, 1037, 819, 775, 875, 609 cm^{-1}; ^{1}H NMR (C_6D_6) δ

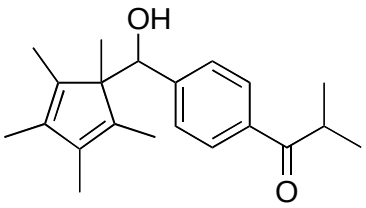
1.03 (s, 3H), 1.27 (s, 1H), 1.40 (d, *J* = 1.5 Hz, 3H), 1.42 (d, *J* = 1.5 Hz, 3H), 1.46 (s, 3H), 1.90 (s, 3H), 4.21 (d, *J* = 8.5 Hz, 1H), 6.85 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (C_6D_6) δ 10.64, 10.73, 11.14, 12.01, 17.79, 60.99, 77.63, 111.20, 119.07, 117.08, 130.40, 136.53, 136.88, 137.17, 139.09, 146.56. Found: C, 80.79; H, 8.16%. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92%. m.p. 99–100 ˚C.

(4-Butoxyphenyl)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methanol (2f)



IR (neat) 3469, 2931, 1612, 1512, 1446, 1244, 1174, 1029, 821, 603 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.80 (t, *J* = 7.5 Hz, 3H), 1.22 (s, 3H), 1.20–1.30 (m, 1H), 1.30 (dq, *J* = 7.5, 7.5 Hz, 2H), 1.51 (s, 3H), 1.54 (dd, *J* = 7.5, 7.5 Hz, 2H), 1.59 (s, 3H), 1.67 (s, 3H), 2.07 (s, 3H), 3.59 (t, *J* = 7.5 Hz, 2H), 4.56 (d, *J* = 3.0 Hz, 1H), 6.77 (d, *J* = 3.5 Hz, 2H), 7.15 (d, *J* = 3.5 Hz, 2H); ^{13}C NMR (C_6D_6) δ 10.94 (× 2), 11.41, 12.24, 13.95, 18.58, 19.49, 31.64, 61.45, 67.35, 78.35, 113.18, 128.29, 134.08, 135.98, 136.07, 138.46, 139.74, 158.78. Found: C, 79.91; H, 9.68%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%.

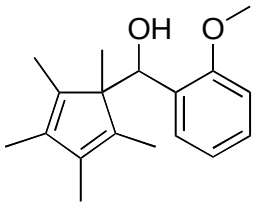
1-{4-[(Hydroxy)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methyl]phenyl}-2-methyl-1-propanone (2g)



IR (neat) 3492, 2872, 1682, 1606, 1382, 1228, 981, 823, 759, 704 cm^{-1}; ^{1}H NMR (C_6D_6) δ 1.06 (d, *J* = 7.0 Hz, 6H), 1.14 (s, 3H), 1.43 (d, *J* = 3.0 Hz, 1H), 1.46 (s, 3H), 1.50 (s, 3H), 1.60 (s, 3H), 2.02 (s, 3H), 3.11 (septet, *J* = 7.0 Hz, 1H), 4.46 (d, *J* = 3.0 Hz, 1H), 7.18 (d, *J* = 8.5 Hz, 2H), 7.81

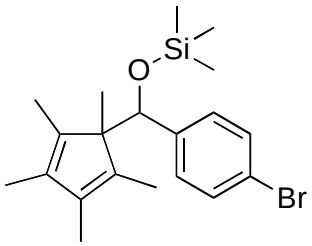
(d, J = 8.5 Hz, 2H); ^{13}C NMR (C_6D_6) δ 10.78, 10.85, 11.27, 12.39, 18.31, 19.21, 19.28, 35.26, 61.29, 78.14, 126.94, 127.10, 134.98, 136.10, 136.41, 137.72, 139.64, 147.46, 203.68. Found: C, 80.71; H, 8.94%. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 8.78%.

(2-Methoxyphenyl)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methanol (2h)



IR (neat) 3469, 2925, 1600, 1587, 1490, 1400, 1240, 1033, 752, 607 cm^{-1}; ^{1}H NMR (C_6D_6) δ 1.30 (s, 3H), 1.57 (d, *J* = 1.0 Hz, 3H), 1.67 (d, *J* = 1.0 Hz, 3H), 1.74 (s, 3H), 1.84 (d, *J* = 4.5 Hz, 1H), 2.08 (s, 3H), 3.26 (s, 3H), 5.39 (d, *J* = 4.5 Hz, 1H), 6.47 (d, *J* = 7.5 Hz, 1H), 6.85 (dd, *J* =7.5, 7.5 Hz, 1H), 7.03 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (C_6D_6) δ 11.04 (× 2), 11.54, 12.08, 18.82, 54.55, 61.89, 71.90, 109.88, 120.02, 128.13, 128.87, 130.65, 135.56, 135.77, 139.49, 140.40, 157.03. Found: C, 79.16; H, 9.02%. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88%.

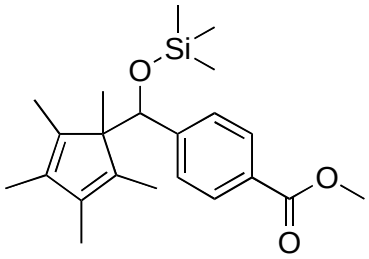
(4-Bromophenyl)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)(trimethylsiloxy)methane (2a-Si)



IR (neat) 841, 889, 1076, 1250, 1377, 1458, 1655, 2924 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ –0.01 (s, 9H), 1.11 (s, 3H), 1.44 (bs, 3H), 1.48 (bs, 3H), 1.79 (s, 3H), 1.93 (s, 3H), 4.56 (s, 1H), 6.83–6.88 (m, 2H), 7.15–7.20 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –0.08, 10.52, 10.64, 10.91, 12.60, 18.07, 60.74, 79.40, 120.02, 127.72, 129.08, 135.77, 136.05, 136.83, 139.29, 140.76. Found: C, 60.84; H,

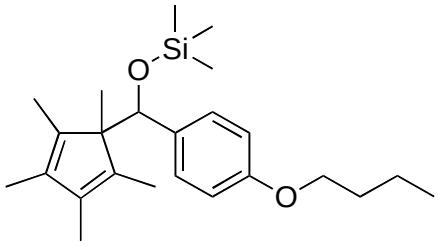
7.33%. Calcd for $C_{20}H_{29}BrOSi$: C, 61.06; H, 7.43%

Methyl 4-[(trimethylsiloxy)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methyl]benzoate (2d-Si)



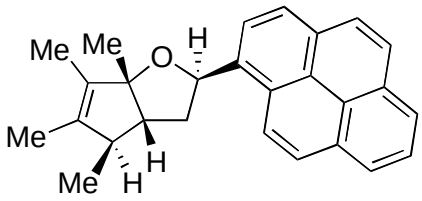
IR (neat) 619, 710, 764, 841, 1076, 1279, 1437, 1611, 1728, 1931, 2957 cm^{-1}; ^1H NMR ($CDCl_3$) δ –0.01 (s, 9H), 1.13 (s, 3H), 1.40 (bs, 3H), 1.43 (bs, 3H), 1.81 (s, 3H), 1.94 (s, 3H), 3.87 (s, 3H), 4.65 (s, 1H), 7.02–7.07 (m, 2H), 7.72–7.76 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –0.11, 10.46, 10.60, 10.94, 12.59, 18.03, 51.87, 60.83, 79.62, 125.96, 127.47, 128.16, 135.75, 136.16, 136.70, 139.30, 147.14, 167.40. Found: C, 70.97; H, 8.49%. Calcd for $C_{22}H_{32}O_3Si$: C, 70.92; H, 8.66%

(4-Butoxyphenyl)(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)(trimethylsiloxy)methane (2f-Si)



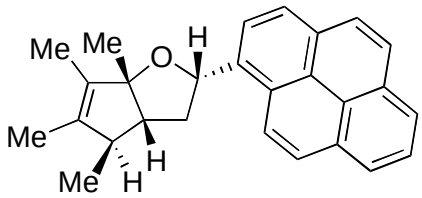
IR (neat) 619, 750, 841, 891, 1070, 1173, 1250, 1512, 1612, 2959 cm^{-1}; ^1H NMR ($CDCl_3$) δ –0.02 (s, 9H), 0.96 (t, *J* = 7.2 Hz, 3H), 1.11 (s, 3H), 1.40–1.52 (m, 8H), 1.67–1.78 (m, 5H), 1.94 (s, 3H), 3.88 (t, *J* = 6.6 Hz, 2H), 4.56 (s, 1H), 6.56–6.62 (m, 2H), 6.83–6.91 (m, 2H); ^{13}C NMR ($CDCl_3$) δ –0.02, 10.59, 10.66, 10.90, 12.67, 13.92, 18.24, 19.26, 31.42, 60.96, 67.44, 79.84, 112.03, 127.11, 133.92, 135.39, 135.41, 137.40, 139.59, 157.58. Found: C, 74.30; H, 9.83%. Calcd for $C_{24}H_{38}O_2Si$: C, 74.55; H, 9.91%

3b



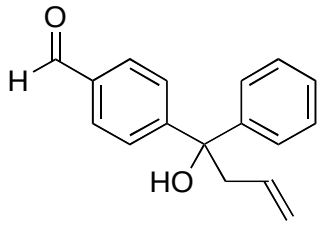
IR (neat) 839, 1074 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.15 (d, *J* = 7.0 Hz, 3H), 1.61 (s, 3H), 1.72 (bs, 3H), 1.74 (bs, 3H), 2.20–2.31 (m, 3H), 2.51 (distorted q, 1H), 5.97 (dd, *J* = 5.5, 10.0 Hz, 1H), 7.96–8.09 (m, 4H), 8.14–8.17 (m, 3H), 8.26–8.29 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 9.73, 12.46, 20.35, 25.07, 43.45, 50.54, 54.79, 75.93, 95.96, 122.93, 123.21, 124.71, 124.75, 124.84, 124.92, 125.09, 125.66, 126.80, 127.10, 127.51, 127.83, 130.39, 130.65, 131.30, 132.51, 135.62, 138.74; Found: C, 88.18; H, 7.21%. Calcd for $C_{27}H_{26}O$: C, 88.48; H, 7.15%. m.p. 131.2–132.4 ˚C.

4b



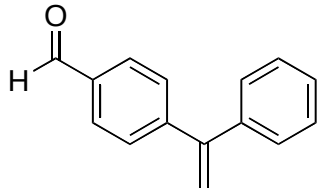
IR (nujol) 852, 1076 cm^{-1}; ^{1}H NMR (500 MHz, ppm, $CDCl_3$) δ 1.11 (d, *J* = 7.0 Hz, 3H), 1.56 (s, 3H), 1.63 (bs, 3H), 1.67–1.74 (m, 1H), 1.87 (bs, 3H), 2.24 (distorted q, 1H), 2.36 (m, 1H), 2.90 (m, 1H), 5.97 (dd, *J* = 5.5, 10.5 Hz, 1H), 7.96–8.09 (m, 4H), 8.14–8.17 (m, 3H), 8.21 (d, *J* = 7.5 Hz, 1H), 8.29 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 9.79, 12.53, 19.63, 25.45, 44.55, 47.99, 56.03, 77.65, 96.41, 122.82, 123.11, 124.69, 124.75, 124.92, 124.95, 125.10, 125.72, 126.75, 127.06, 127.51, 127.60, 130.33, 130.67, 131.37, 134.56, 135.19, 136.51; Found: C, 88.49; H, 7.14%. Calcd for $C_{27}H_{26}O$: C, 88.48; H, 7.15%. m.p. 159.4–160.8 ˚C.

4-(1-Hydroxy-1-phenyl-3-butenyl)benzaldehyde (7c)



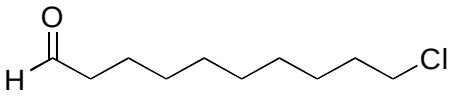
IR (neat) 3477, 3060, 2839, 1699, 1606, 1573, 1446, 1213, 1174, 1062, 991, 825, 731, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.69 (s, 1H), 3.07 (dd, *J* = 7.2, 14.1 Hz, 1H), 3.15 (dd, *J* = 7.2, 14.1 Hz, 1H), 5.19–5.30 (m, 2H), 5.58–5.73 (m, 1H), 7.22–7.28 (m, 2H), 7.31–7.36 (m, 2H), 7.44–7.49 (m, 2H), 7.62–7.66 (m, 2H), 7.81–7.84 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 46.34, 76.81, 121.18, 125.88, 126.56, 127.32, 128.44, 129.68, 132.62, 134.94, 145.53, 153.28, 191.92. Found: C, 80.69; H, 6.55%. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39%.

4-(1-Phenylethenyl)benzaldehyde (9)



IR (neat) 3028, 2829, 2734, 1697, 1604, 1566, 1211, 1168, 840, 779, 704 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.58 (d, *J* = 1.0 Hz, 1H), 5.59 (d, *J* = 1.0 Hz, 1H), 7.30–7.38 (m, 5H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.86 (d, *J* = 8.0 Hz, 2H), 10.03 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 116.48, 128.08, 128.16, 128.35, 128.79, 129.66, 135.59, 140.53, 147.59, 149.12, 191.80. Found: C, 86.28; H, 5.81%. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81%.

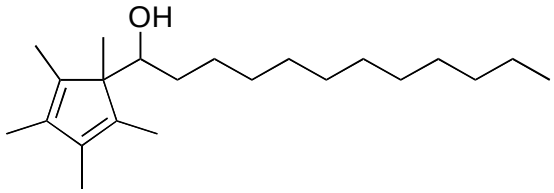
10-Chlorodecanal (10f)



IR (neat) 650, 723, 1356, 1466, 1726, 2719, 2930, 3429 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.24–1.82 (m, 14H), 2.92 (td, *J* = 7.2, 1.8 Hz, 2H), 3.53 (t, *J* = 6.6 Hz, 2H), 9.76 (t, *J* = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 22.00, 26.79, 28.76, 29.07, 29.20 (× 2), 32.56, 43.87, 45.15, 202.95. HRMS [$M+H^+$]

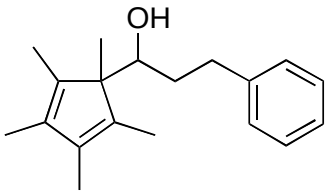
found: 191.1203. Calcd for $C_{10}H_{20}ClO$: 191.1202.

1-(1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl)-1-dodecanol (11a)



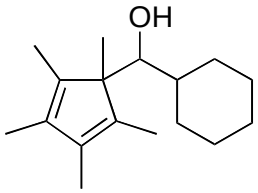
IR (neat) 1013, 1379, 1445, 1657, 2924, 3483 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.6 Hz, 3H), 1.02 (s, 3H), 1.05–1.53 (m, 21H), 1.70 (s, 3H), 1.76 (brs, 6H), 1.79 (s, 3H), 3.54 (dt, *J* = 7.2, 4.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.93 (× 2), 11.05, 11.40, 14.12, 18.21, 22.69, 27.25, 29.34, 29.63 (× 2), 29.65, 29.69, 29.71, 31.56, 31.91, 60.34, 75.96, 135.12, 135.33, 138.69, 139.87. Found: C, 82.05; H, 12.67%. Calcd for $C_{22}H_{40}O$: C, 82.43; H, 12.58%.

1-(1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl)-3-phenyl-1-propanol (11b)



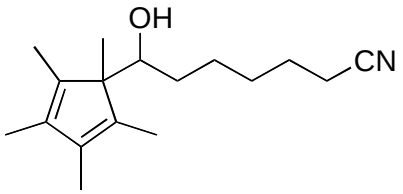
IR (neat) 700, 1030, 1454, 2920, 3483 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (s, 3H), 1.34–1.47 (m, 3H), 1.59 (s, 3H), 1.74 (brs, 6H), 1.80 (s, 3H), 2.54 (dt, *J* = 13.8, 7.8 Hz, 1H), 2.82 (dt, *J* = 13.8, 7.8 Hz, 1H), 3.48–3.62 (m, 1H), 7.10–7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 10.84, 11.07, 11.20, 11.62 ,18.30, 33.44, 33.50, 60.27, 75.21, 125.57, 128.16 (× 2), 128.41 (× 2), 135.12, 135.28, 138.44, 139.59, 142.32. Found: C, 84.59; H, 9.97%. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69%.

1-Cyclohexyl-1-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)methanol (11c)



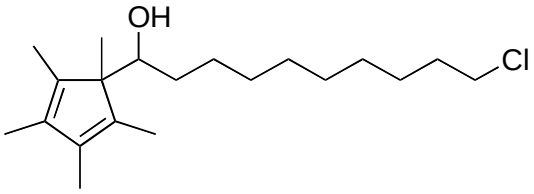
IR (neat) 974, 1379, 1448, 1655, 2922, 3504 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.99–1.58 (m, 15H), 1.66 (s, 3H), 1.71 (brs, 6H), 2.04 (s, 3H), 3.35 (d, *J* = 5.1 Hz, 1H); ^{13}C NMR (C_6D_6) δ 10.87, 11.35, 11.51, 13.41, 21.32, 27.14, 27.18, 27.61, 27.87, 33.37, 40.86, 61.04, 81.52, 134.81, 134.90, 140.13, 142.13. Found: C, 82.10; H, 11.53%. Calcd for $C_{17}H_{28}O$: C, 82.10; H, 11.36%.

7-Hydroxy-7-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)heptanenitrile (11e)



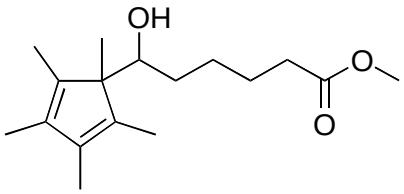
IR (neat) 1059, 1379, 1445, 1657, 2247, 2932, 3520 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.02 (s, 3H), 1.10–1.67 (m, 9H), 1.70 (s, 3H), 1.76 (brs, 6H), 1.79 (s, 3H), 2.32 (t, *J* = 7.2 Hz, 2H), 3.53 (dt, *J* = 7.5, 4.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.93, 10.94, 11.07, 11.37, 17.08, 18.14, 25.38, 26.43, 28.67, 31.14, 60.27, 75.77, 119.85, 135.33, 135.58, 138.46, 139.69. HRMS [M+H] found: 261.2094. Calcd for $C_{17}H_{28}NO$: 261.2093.

10-Chloro-1-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-1-decanol (11f)



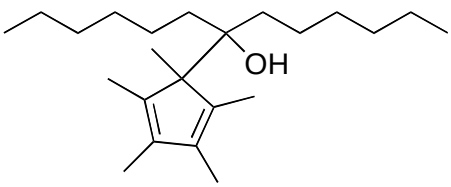
IR (neat) 1036, 1379, 1447, 2926, 3449 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.97–1.66 (m, 20H), 1.70 (s, 3H), 1.71 (s, 3H), 1.73 (s, 3H), 1.97 (s, 3H), 3.11 (t, *J* = 6.9 Hz, 2H), 3.45–3.55 (m, 1H); ^{13}C NMR (C_6D_6) δ 10.62, 10.97, 11.13, 12.14, 18.75, 27.04, 27.51, 29.08, 29.74, 29.98, 30.03, 31.88, 32.81, 44.93, 60.80, 75.99, 134.97, 135.07, 139.21, 140.91. HRMS [M+H] Found: 326.2376. Calcd for $C_{20}H_{36}ClO$: 326.2376.

Methyl 6-hydroxy-6-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)hexanoate (11g)



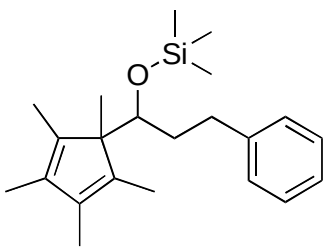
IR (nujol) 1377, 1462, 1724, 2361, 2853, 3520 cm^{-1}; ^{1}H NMR (C_6D_6) δ 1.05 (s, 3H), 1.07–1.60 (m, 7H), 1.64 (s, 3H), 1.69 (s, 3H), 1.71 (s, 3H), 1.94 (s, 3H), 2.07 (t, *J* = 7.2 Hz, 2H), 3.33 (s, 3H), 3.37–3.45 (m, 1H); ^{13}C NMR (C_6D_6) δ 10.55, 10.94, 11.10, 12.10, 18.70, 25.05, 26.75, 31.29, 34.09, 50.88, 60.71, 75.53, 134.93, 135.04, 139.14, 140.87, 173.41. Found: C, 72.52; H, 10.11%. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06%. m.p. 63–65 ˚C.

7-(1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl)-7-tridecanol (16)



IR (neat) 523, 621, 725, 935, 1036, 1136, 1379, 1456, 1653, 1715, 2926, 3508 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.91 (t, *J* = 6.3 Hz, 6H), 0.97 (s, 1H), 1.18 (s, 3H), 1.20–1.64 (m, 20H), 1.74 (s, 6H), 1.98 (s, 6H); ^{13}C NMR (C_6D_6) δ 11.23 (× 2), 13.94 (× 2), 14.30 (× 2), 17.03, 23.02 (× 2), 24.63 (× 2), 30.61 (× 2), 32.23 (× 2), 37.12 (× 2), 64.38, 77.62, 135.51 (× 2), 141.69 (× 2). HRMS [M–OH] Found: 317.3203. Calcd for $C_{23}H_{41}$: 317.3210.

1-(1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl)-3-phenyl-1-(trimethylsilyloxy)propane (The trimethylsilyl ether of 11b)



IR (neat) 511, 698, 748, 866, 1059, 1250, 1447, 1605, 1657, 1938, 2957 cm^{-1}; ^{1}H NMR (C_6D_6)

δ 0.24 (s, 9H), 1.12 (s, 3H), 1.43–1.51 (m, 1H), 1.54–1.62 (m, 4H), 1.67 (s, 3H), 1.70 (s, 3H), 2.06 (s, 3H), 2.49 (ddd, *J* = 13.5, 10.0, 7.0 Hz, 1H), 2.80 (ddd, *J* = 13.5, 10.5, 5.0 Hz, 1H), 3.80 (dd, *J* = 8.0, 2.5 Hz, 1H), 6.99–7.03 (m, 1H), 7.07–7.13 (m, 4H); ^{13}C NMR (C_6D_6) δ 0.96 (× 3), 10.16, 10.92, 11.07, 12.49, 20.25, 33.78, 34.98, 60.90, 77.39, 125.96, 128.62 (× 2), 128.70 (× 2), 134.88, 134.93, 139.19, 141.50, 142.93. Found: C, 77.38; H, 10.18%. Calcd for $C_{22}H_{34}Si$: C, 77.13; H, 10.00%.

Table S1. Coordinates of atoms in acetone optimized at the RHF/6-311+G** level
Total Energy (au): –193.2170126 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
O	0	0	1.8284909161
C	0	0	0.64015737136
C	-1.2870752934	0	-0.15492180701
H	-1.3274600248	-0.87541943607	-0.79738388578
H	-1.3274600248	0.87541943607	-0.79738388578
H	-2.1354789018	0	0.51536543486
C	1.2870752934	0	-0.15492180701
H	1.3274600248	-0.87541943607	-0.79738388578
H	2.1354789018	0	0.51536543486
H	1.3274600248	0.87541943607	-0.79738388578

Table S2. Coordinates of atoms in **Adduct A** optimized at the RHF/6-311+G** level

Total Energy (au): –583.9946700 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	-0.4794419563	-1.1522606954	-0.20998966494
C	-1.69879071	-0.68826018296	0.051592604571
C	-1.6824773022	0.7965765523	0.057985933949
C	-0.45074564753	1.2261985289	-0.20262636156
C	0.49557127027	0.026525508953	-0.3843225294
C	-0.019344730398	2.6635513165	-0.29716521261
H	-0.87174697428	3.315225384	-0.43967090667
H	0.65163506864	2.8287443383	-1.1343916974
H	0.49309443643	2.9811553009	0.60565293762
C	-2.9264065946	1.5993364695	0.32228372059
H	-3.7117375737	1.350391198	-0.38711645613
H	-2.7484736813	2.6639376551	0.25948146097
H	-3.3158025748	1.391710161	1.3163493047
C	-2.9615777579	-1.481986239	0.23955391692
H	-3.6767819157	-1.2728353081	-0.55284366528
H	-3.444217069	-1.2283780534	1.1797642776
H	-2.771060587	-2.5472057482	0.24594615945
C	-0.15058181825	-2.6036256158	-0.48433199217
H	-0.94135543341	-3.0681766818	-1.0635557854
H	-0.031123874204	-3.1867155489	0.42442811843
H	0.76319341793	-2.7096133473	-1.053907834
C	1.0470327409	0.0094064649314	-1.8259130322
H	0.22537021327	-0.073785383862	-2.529954005
H	1.71689599	-0.82755710387	-1.9951194184
H	1.5938028543	0.91501512498	-2.058896259
C	1.6540080703	0.042052195166	0.69535694842
C	2.7743772268	1.037190569	0.37509926618
H	2.4113471617	2.0302208474	0.16071416577
H	3.3706858346	0.69857790079	-0.46490299883
H	3.4225932749	1.1030646802	1.2418611381
C	2.3186639102	-1.3248375434	0.91071774544
H	1.6331268313	-2.0357351158	1.3514629565
H	3.1442976613	-1.1984448905	1.602753145
H	2.7135928776	-1.7458914659	-0.0077078278033
O	1.1284268026	0.46237265478	1.93840846
H	0.3239505575	0.0040560736592	2.1129992173

Table S3. Coordinates of atoms in **TS A** optimized at the RHF/6-311+G** level

Total Energy (au): –583.9480580 (B3LYP/6-311+G**//RHF/6-311+G**)

Imaginary Frequency (cm^{-1}): –1022.10 (RHF/6-311+G**)

atom	x	y	z
C	-0.36036086418	-1.1461981789	-0.66982919121
C	-1.5089751124	-0.6951102842	0.0011902890445
C	-1.5403143313	0.75672611318	-0.11724649315
C	-0.38868215571	1.1566534174	-0.72257706417
C	0.41040220654	-0.027370069172	-1.00605644
C	0.019920563472	2.5522958033	-1.1117135184
H	-0.62881067773	3.3005569924	-0.6723747497
H	-0.020898424206	2.6827552149	-2.1918635942
H	1.0365890229	2.7876974126	-0.80892257562
C	-2.6590827287	1.604336506	0.42290911488
H	-3.6103933727	1.3422762745	-0.035562272869
H	-2.4909631218	2.6585962916	0.24059357663
H	-2.7741860402	1.4731514866	1.4970808986
C	-2.7001151199	-1.5406939324	0.38906815221
H	-3.4207142608	-1.6127993628	-0.42505940035
H	-3.2239807904	-1.1260937293	1.2451930268
H	-2.4061024853	-2.552138057	0.65027054694
C	-0.040666304349	-2.5903191251	-0.95153317099
H	-0.66994646211	-2.97403041	-1.7522919456
H	-0.21303337993	-3.223293941	-0.08462945231
H	0.98860537095	-2.7295422563	-1.2598711759
C	1.6209059994	-0.010199657809	-1.9056105472
H	1.3366163116	0.18672564495	-2.9383270347
H	2.1519422835	-0.95530767522	-1.8976612352
H	2.330027898	0.76553815017	-1.6262442024
C	1.3039969655	-0.029507309081	1.4002792613
C	1.9225827981	1.3323994404	1.4938291122
H	1.1612469591	2.0953566528	1.5304645952
H	2.6176497217	1.5223856309	0.68645378481
H	2.4868127194	1.3580649447	2.4271522962
C	2.2323802997	-1.1981055224	1.2396974115
H	1.6888592796	-2.1194806001	1.1043989598
H	2.797337277	-1.2706164586	2.17083951
H	2.9395890561	-1.0518070534	0.43493247786
O	0.19050564774	-0.20159114846	1.9722458931
H	-0.57874474845	-0.52131120517	1.270740716

Table S4. Coordinates of atoms in Cp*H of **Products A** optimized at the RHF/6-311+G** level Total Energy (au): –390.7936835 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	-0.21955564177	-0.31179038052	1.1853181893
C	-0.032854140365	0.93145544395	0.74659799452
C	-0.032854140365	0.93145544395	-0.74659799452
C	-0.21955564177	-0.31179038052	-1.1853181893
C	-0.35695437763	-1.2438786135	0
H	-1.3624155091	-1.6718645992	0
C	0.14868099624	2.1912929162	-1.5459001561
H	-0.62978514134	2.9150557292	-1.3171060814
H	0.12132960916	2.0017462122	-2.6110147764
H	1.1017260771	2.6626094621	-1.3186241497
C	-0.31135983213	-0.81831888253	-2.5957243311
H	-0.31176435189	-0.01259082564	-3.3189372121
H	-1.2238190234	-1.3926180705	-2.7413533021
H	0.52121945439	-1.475761796	-2.8362911455
C	0.65609214765	-2.3971878485	0
H	0.53154771925	-3.0277465279	0.87492289754
H	1.6725462887	-2.0137354997	0
H	0.53154771925	-3.0277465279	-0.87492289754
C	-0.31135983213	-0.81831888253	2.5957243311
H	-1.2238190234	-1.3926180705	2.7413533021
H	-0.31176435189	-0.01259082564	3.3189372121
H	0.52121945439	-1.475761796	2.8362911455
C	0.14868099624	2.1912929162	1.5459001561
H	-0.62978514134	2.9150557292	1.3171060814
H	1.1017260771	2.6626094621	1.3186241497
H	0.12132960916	2.0017462122	2.6110147764

Table S5. Coordinates of atoms in **Adduct B** optimized at the RHF/6-311+G** level

Total Energy (au): –544.6750327 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	-0.40746572714	-1.1582278869	-0.34455636052
C	-1.6187078192	-0.69323273142	-0.046174147174
C	-1.5961400821	0.79478373197	-0.033929714011
C	-0.37244287998	1.2212470354	-0.33785841514
C	0.55179902214	0.018123621611	-0.52429392868
C	0.073533636325	2.6492209838	-0.48044590963
H	-0.77404484345	3.321446811	-0.51514280372
H	0.63692338022	2.7935695024	-1.3984403658
H	0.70556141708	2.9508883282	0.3483578667
C	-2.8301143634	1.6024825423	0.25855191719
H	-3.6247773175	1.3746033652	-0.44769357151
H	-2.6420212685	2.6663758376	0.21355622058
H	-3.2114093291	1.3792122751	1.2521785821
C	-2.8821487038	-1.4781183833	0.16928529619
H	-3.6211420439	-1.2493884709	-0.59530404741
H	-3.3298188926	-1.2343603046	1.1293054838
H	-2.7024433013	-2.5451623268	0.1543672285
C	-0.066714276481	-2.5924097198	-0.67434773928
H	-0.92682258994	-3.1021965213	-1.0927845923
H	0.26446554848	-3.166883773	0.18520559109
H	0.72307925743	-2.6401106878	-1.4165210777
C	1.8176764438	0.060348193152	0.404949928
C	2.9068287648	0.9550159042	-0.18995072207
H	2.5547865092	1.9537615762	-0.39942839442
H	3.2866761927	0.52403902985	-1.1119213462
H	3.7283839765	1.0327731375	0.51402825304
C	2.4370345006	-1.3169758858	0.66230324544
H	1.7720176262	-1.9478000663	1.238615412
H	3.3460916949	-1.1857998033	1.2393252574
H	2.6910876855	-1.8306757147	-0.25917935675
O	1.4870528124	0.62900694351	1.6556590479
H	0.71062490346	0.21829926765	1.9962635469
H	0.91259006675	-0.0038558110074	-1.553983845

Table S6. Coordinates of atoms in **TS B** optimized at the RHF/6-311+G** level

Total Energy (au): –544.6221616 (B3LYP/6-311+G**//RHF/6-311+G**)

Imaginary Frequency (cm^{-1}): –1178.03 (RHF/6-311+G**)

atom	x	y	z
C	-0.33255788066	-1.1640001179	-0.80838904924
C	-1.3543701541	-0.70518103682	0.040581757473
C	-1.4036342378	0.74886781493	-0.086699010742
C	-0.36468202924	1.141979262	-0.87231597785
C	0.36918599301	-0.046330769603	-1.2547680557
C	-0.0098298730264	2.5362780002	-1.3189460662
H	-0.21946534988	3.2834339054	-0.55944122621
H	-0.5673163407	2.8158980167	-2.2105707473
H	1.0437146305	2.6116175632	-1.5713390836
C	-2.4165015736	1.6149558036	0.60899141467
H	-3.4306846295	1.3626854438	0.30567704255
H	-2.2623879067	2.6638917572	0.38390756591
H	-2.3670227071	1.4998789413	1.6901660643
C	-2.4675461378	-1.5451149507	0.62211412458
H	-3.319668559	-1.6002650557	-0.054351200543
H	-2.8290730263	-1.1379792328	1.5619336523
H	-2.1402588388	-2.5619551673	0.81465992107
C	-0.030227438474	-2.5999017782	-1.1393645777
H	-0.81439330264	-3.0245428549	-1.7618547377
H	0.043339985419	-3.2266449716	-0.25328407397
H	0.90126224681	-2.686014744	-1.6892530117
C	1.6748669512	-0.020341914605	0.91520268899
C	2.28200484	1.3513540822	0.8941459662
H	1.5262020291	2.1064403622	1.0399472586
H	2.8373193414	1.5373044974	-0.015362677856
H	2.9828787732	1.3951880402	1.7289375731
C	2.5756777907	-1.1760982589	0.58325296751
H	2.0286348713	-2.1037358513	0.53864404908
H	3.2967689094	-1.2457629041	1.399660501
H	3.1240130545	-1.0154798491	-0.3348217581
O	0.68203244132	-0.20790504997	1.6685378388
H	-0.21094734371	-0.53634462303	1.1057082915
H	1.1726654713	-0.066174359525	-1.971304233

Table S7. Coordinates of atoms in tetramethylcyclopentadiene of **Products B** optimized at the RHF/6-311+G** level

Total Energy (au): –351.4662604 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	0.63344245562	-0.69370384383	0.34168220562
C	-0.85529912116	-0.42651262333	0.20643189247
C	-1.0526607307	0.87438924396	-0.0053019474415
C	0.26214997917	1.5577105324	-0.02535515462
H	0.38317363628	2.6176136861	-0.17070062493
C	1.2417856723	0.6836479648	0.17115841389
C	2.715120293	0.95181945046	0.23921778744
H	3.251384075	0.43502006378	-0.55310212659
H	3.1330319	0.6125146974	1.1845540106
H	2.9186068657	2.0126761679	0.14325093024
C	-2.3347844176	1.6311545232	-0.19557971423
H	-2.3399107092	2.1371849793	-1.15840871
H	-2.4450018834	2.396109843	0.56979396421
H	-3.2041152443	0.98748666076	-0.15315952798
C	-1.8654851257	-1.5306530276	0.32698628544
H	-1.7652919014	-2.2514267716	-0.48154541298
H	-2.8805206522	-1.1538614096	0.30580075641
H	-1.7355200182	-2.0760789542	1.2595025935
H	0.84101360801	-1.0472604266	1.3544106624
C	1.1723628089	-1.7320369756	-0.65204449935
H	0.69718215843	-2.6968838428	-0.50487175094
H	2.2417272471	-1.8736310718	-0.52813807647
H	0.98760910428	-1.415278866	-1.6745819567

Table S8. Coordinates of atoms in **Adduct C** optimized at the RHF/6-311+G** level

Total Energy (au): –387.3703919 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	-1.313566774	-1.1248987392	-0.34958068069
C	-2.5259829963	-0.70289683872	-0.0059297872541
C	-2.5238516199	0.77127199455	0.069328399094
C	-1.3094310027	1.2172954905	-0.22729442213
C	-0.38915263799	0.059890016201	-0.54680752285
C	0.9355738235	0.01570321689	0.26036089329
C	1.7784579563	1.2606296838	-0.0048483597667
H	1.2557117041	2.1577871662	0.30269256192
H	2.0310371585	1.3436176529	-1.0581224337
H	2.6994873008	1.2032428511	0.56531744072
C	1.7442631118	-1.2362445634	-0.096857709308
H	1.2165807288	-2.1428401159	0.1798599951
H	2.6855625917	-1.2258528513	0.44207920657
H	1.9582073537	-1.2791467437	-1.1613149552
O	0.67269489636	0.026236151096	1.6451261559
H	0.0034511023977	-0.60240280395	1.8546900536
H	-3.377852667	1.3704652964	0.32424549398
H	-3.3858842626	-1.3220385269	0.17201037503
H	-1.0076308777	2.2459419177	-0.25102814577
H	-0.12010708805	0.11088491858	-1.603425278
H	-1.0275678016	-2.1466451727	-0.51050128055

Table S9. Coordinates of atoms in **TS C** optimized at the RHF/6-311+G** level

Total Energy (au): –387.3130760 (B3LYP/6-311+G**//RHF/6-311+G**)

Imaginary Frequency (cm^{-1}): –627.09 (RHF/6-311+G**)

atom	x	y	z
C	-1.365980052	1.1185080435	0.61435619218
C	-2.0774007119	0.66244196399	-0.51502694099
C	-2.1930618555	-0.76259329454	-0.3900845601
C	-1.4899021068	-1.156329859	0.72031114384
C	-0.93683923096	0.0089996301282	1.3346445001
C	1.1597245641	-0.022904023837	-0.5326618144
C	1.8640640415	-1.2962956119	-0.18924733908
H	1.2303449616	-2.1418311341	-0.40804908263
H	2.178729318	-1.3083713777	0.84561811858
H	2.7554518686	-1.3466939981	-0.81500236403
C	1.7224316153	1.2720237377	-0.034892427787
H	1.0847427868	2.1039971407	-0.28479381877
H	2.6782473827	1.3915976063	-0.54871325913
H	1.9141800193	1.2437591428	1.0278038062
O	0.34494968669	-0.05172815498	-1.474948214
H	-0.60107415619	0.40317831826	-1.2585073666
H	-2.6449618287	1.2781607986	-1.1897163733
H	-2.7016909844	-1.4069083409	-1.0826814989
H	-1.1710773748	2.1468847344	0.85790620924
H	-0.39318157391	0.030795910645	2.2624507949
H	-1.3576963694	-2.166691232	1.0612342946

Table S10. Coordinates of atoms in cyclopentadiene of **Products C** optimized at the RHF/6-311+G** level

Total Energy (au): –194.1551940 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	0.18443185863	-0.0022213760959	1.1740431657
C	-1.0715272256	0.012744101108	0.73812561472
C	-1.0715272256	0.012744101108	-0.73812561472
C	0.18443185863	-0.0022213760959	-1.1740431657
C	1.126552879	-0.013407815472	0
H	1.7646713284	-0.89615662517	0
H	0.50517862967	-0.0059501382376	-2.1987163253
H	1.7854314422	0.85395603616	0
H	0.50517862967	-0.0059501382376	2.1987163253
H	-1.9564110876	0.023231615468	1.3470217198
H	-1.9564110876	0.023231615468	-1.3470217198

Table S11. Coordinates of atoms in **Adduct D** optimized at the RHF/6-311+G** level

Total Energy (au): –585.2079615 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	-0.63280615358	-1.1148553556	-0.29982114538
C	-1.7845119803	-0.47670113316	-0.13358848767
C	0.55363966001	-0.15735324799	-0.52579707886
C	-3.1322440535	-1.1022046995	0.10270086792
H	-3.8299154906	-0.81145536224	-0.68062033346
H	-3.5575772172	-0.7663487468	1.045202217
H	-3.0885549002	-2.1837052816	0.12937514863
C	-0.51082465703	-2.6269574397	-0.36653444307
H	-1.2053784934	-3.0303331925	-1.0969937462
H	-0.73062774912	-3.1023781359	0.58489262148
H	0.47954283706	-2.9429284387	-0.66224125437
C	1.3773868388	-0.58589704206	-1.7589868367
H	0.71405496997	-0.83694183663	-2.5808089194
H	2.0077732277	-1.4485358711	-1.5727092054
H	2.0220095813	0.21972267299	-2.0945737202
C	1.486652331	-0.084462623382	0.74798375944
C	2.7865588413	0.69596876854	0.52296189104
H	2.6233985835	1.6868313471	0.13158659326
H	3.4493135919	0.16481891531	-0.15053468615
H	3.290214855	0.79734956735	1.477880122
C	1.8877991704	-1.4664727961	1.2914950015
H	1.0307132296	-2.0211258835	1.6530823017
H	2.5577000038	-1.320932206	2.1321191606
H	2.4024630393	-2.0748265244	0.55669314576
O	0.81755025673	0.59331434112	1.7922713861
H	0.052450710296	0.10059325831	2.0325609572
C	-1.6628725797	1.0199341925	-0.30741689328
C	-0.23110367707	1.1630774874	-0.89001815154
H	-2.3656408098	1.3215395681	-1.0862260361
H	-0.37659581643	1.0679267488	-1.963115854
C	-2.0400045737	1.8544644395	0.92576561389
H	-1.3935558293	1.6760487891	1.7745948546
H	-3.0622906288	1.6377206422	1.224135975
H	-1.9947883801	2.9152105156	0.69986558337
C	0.4037010711	2.5392402849	-0.68761132248
H	1.3179797014	2.6443388653	-1.2629288498
H	0.62029950909	2.7566382343	0.34949908368
H	-0.28190901925	3.2996771782	-1.0541369427

Table S12. Coordinates of atoms in **TS D** optimized at the RHF/6-311+G** level

Total Energy (au): –585.1436305 (B3LYP/6-311+G**//RHF/6-311+G**)

Imaginary Frequency (cm^{-1}): –1902.52 (RHF/6-311+G**)

atom	x	y	z
C	-0.31507651842	-1.1750657581	-0.56572158208
C	-1.4825496086	-0.75201787029	0.092360564949
C	0.53163734016	-0.072641908997	-0.80095772499
C	-2.6596759334	-1.6654680102	0.37082688041
H	-3.2587272247	-1.8264469764	-0.525159252
H	-3.3111524934	-1.2304312009	1.121194414
H	-2.3485762074	-2.6359208046	0.74260520111
C	0.020482352185	-2.6235134566	-0.76361415126
H	-0.67040070296	-3.0386504567	-1.4941142151
H	-0.11211634851	-3.1858962102	0.15474081482
H	1.0261177051	-2.7799808295	-1.1245877247
C	1.7096135657	-0.15300914612	-1.7528788573
H	1.3703647348	-0.070529498461	-2.7851651733
H	2.2644574368	-1.0779230087	-1.6652234984
H	2.4099907783	0.65901520533	-1.5892033698
C	1.2751368505	-0.064478093759	1.1821665401
C	1.9445297341	1.2973515304	1.2987922548
H	2.539735059	1.5701207212	0.43679694268
H	2.6138605449	1.2472077459	2.1561315171
H	1.2168048261	2.0646670293	1.5037503708
C	2.2914973868	-1.1997216268	1.2046705267
H	1.8251367471	-2.1657759617	1.07791237
H	2.7478745348	-1.1912798089	2.1924780244
H	3.0823819027	-1.0764053206	0.47463917062
O	0.24737734867	-0.23208518091	1.9253873814
H	-0.72970777689	-0.60021982744	1.1757402295
C	-1.7551731637	0.70852305545	-0.30148529965
C	-0.45497092321	1.0964517969	-1.0732066989
H	-2.5837480539	0.7180141084	-1.0103528755
H	-0.68805529965	0.96977533936	-2.1318069784
C	-2.1747276746	1.6131011374	0.86162477225
H	-1.4125547381	1.6790958891	1.6271141683
H	-3.0745483811	1.2213975549	1.328765709
H	-2.4077292438	2.6149584802	0.51221269137
C	0.00057016849536	2.5531906635	-0.96671701908
H	0.95021818024	2.7031848311	-1.4724598243
H	0.099430680101	2.9118621617	0.046053638371
H	-0.72772758424	3.1895437056	-1.4633057996

Table S13. Coordinates of atoms in pentamethylcyclopentene of **Products D** optimized at the RHF/6-311+G** level

Total Energy (au): –392.0107116 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	1.9182721902	1.3755845696	1.1269561639
H	1.914637983	2.4562314754	1.245017039
H	2.950695936	1.0646750213	0.99501645306
C	2.2300518677	-1.2539416815	-0.80249478005
H	3.0852650131	-1.1249947167	-0.14327795644
H	2.5086116832	-0.83802866964	-1.7686298852
H	2.0714131134	-2.3166775623	-0.93313436173
C	-0.53119987369	-2.5202472053	0.17226411469
H	-0.82375844661	-2.8017230292	1.1823106578
H	0.27397206776	-3.1760421697	-0.13236545324
H	-1.3839906791	-2.7182753266	-0.47188728103
C	-0.44836463728	1.3173140141	0.11880152238
C	-1.0821296822	0.0035360420115	0.64875781943
H	-0.56141029855	2.1066962799	0.8583792432
H	-1.0049541467	0.0050060649245	1.7383116736
C	-1.0513327819	1.8220399442	-1.1961125876
H	-0.96188803163	1.0823201744	-1.9872573752
H	-0.52935956406	2.7179976854	-1.5215557639
H	-2.1009521259	2.0770333512	-1.0925204388
C	-2.5627674023	-0.20864151837	0.32182244658
H	-2.9395191484	-1.1036873158	0.80765267468
H	-2.7384105035	-0.31286815484	-0.74432642174
H	-3.1586193723	0.62682521603	0.67936663347
H	1.5550177197	0.93485489142	2.0517310768
C	1.0453953798	0.95720582299	-0.065080401141
H	1.4447274114	1.4471205404	-0.9527665002
C	1.0178760612	-0.54893228227	-0.26152469056
C	-0.13727973236	-1.0703814611	0.12654637807

Table S14. Coordinates of atoms in **Adduct E** optimized at the RHF/6-311+G** level

Total Energy (au): –585.2122423 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	-0.2450539793	-1.0559686376	-0.40333041796
C	-1.4233381323	-0.89285886255	0.18140593052
C	0.62595508075	0.20854878814	-0.31921915113
C	-2.502060018	-1.9314048351	0.3256809478
H	-3.3909458917	-1.6570416728	-0.23677416478
H	-2.8041818308	-2.0273551904	1.3668789878
H	-2.1796654808	-2.9059879921	-0.018349497568
C	0.18364424613	-2.3243487654	-1.1172104345
H	-0.50503425276	-2.5617272675	-1.9230959921
H	0.20557434615	-3.1801925132	-0.44804076398
H	1.1677357745	-2.235817573	-1.5552214788
C	1.3076523225	0.49454513836	-1.6725621504
H	0.58998611652	0.45255332308	-2.4835625491
H	2.0812439341	-0.23064132268	-1.8939834299
H	1.7714146379	1.4728669157	-1.6945963656
C	1.7242333676	0.086752137014	0.8122194202
C	2.6269457972	1.3220672919	0.88525402857
H	2.0603439034	2.2439725965	0.92660880998
H	3.301529701	1.3716791478	0.038319675219
H	3.223573063	1.2599848044	1.7884531658
C	2.6206522526	-1.1543990303	0.68442121801
H	2.0492286043	-2.0705195324	0.78265029982
H	3.3486092776	-1.1371578542	1.4886276857
H	3.1616669911	-1.189726408	-0.25406116682
O	1.0993576394	0.021720544987	2.0803127896
H	0.55164870888	-0.74322729399	2.1168338044
C	-1.5982076914	0.50112336076	0.75025423749
C	-0.44099050102	1.2991520838	0.084710047764
H	-1.4106489603	0.46271315426	1.8212339525
H	-0.018271795089	1.9677866645	0.82234614337
C	-3.0103411986	1.0763862248	0.59172232615
H	-3.3425729866	1.0960641763	-0.44144908545
H	-3.0602660662	2.0893774318	0.9805148035
H	-3.723727626	0.48329955463	1.1563461086
C	-0.91837137308	2.17036732	-1.0849952703
H	-0.097553019895	2.7257279637	-1.523914614
H	-1.6418997742	2.9003040879	-0.73965177483
H	-1.3878651865	1.5913820408	-1.8747759524

Table S15. Coordinates of atoms in **TS E** optimized at the RHF/6-311+G** level

Total Energy (au): –585.1515935 (B3LYP/6-311+G**//RHF/6-311+G**)

Imaginary Frequency (cm^{-1}): –1908.55 (RHF/6-311+G**)

atom	x	y	z
C	-0.13495504834	-0.87286205381	-0.66728242301
C	-1.0888652749	-1.0054642118	0.35173811582
C	0.49153855057	0.38122875968	-0.58264049727
C	-2.0201502642	-2.1938456045	0.48724238409
H	-2.8655415497	-2.1369026377	-0.19585926186
H	-2.4199444718	-2.250584434	1.4950083261
H	-1.5038965833	-3.1284551341	0.29601413675
C	0.2989923934	-2.0233843316	-1.5289478307
H	-0.525965617	-2.3164246044	-2.1733301305
H	0.55410321166	-2.8877286172	-0.92354481301
H	1.1449585177	-1.7800272089	-2.1554164966
C	1.4070011468	0.90417470949	-1.6738049738
H	0.84955249403	1.188807434	-2.5624434333
H	2.1447388791	0.17463023578	-1.9796404972
H	1.9434228665	1.7883981459	-1.3428045352
C	1.732323776	-0.16327366234	1.0877957774
C	2.0944713966	1.2009598928	1.6504932205
H	1.2706970935	1.6200907819	2.209945761
H	2.4277163419	1.9058374378	0.89823820024
H	2.9175839288	1.0491533492	2.3469497288
C	2.9109692276	-0.88358703559	0.45142304033
H	2.603846347	-1.7912791629	-0.050088480763
H	3.580601337	-1.1709164893	1.2597879091
H	3.4694275677	-0.25938537052	-0.2345886159
O	0.98561407829	-0.88190403441	1.8324537752
H	-0.072943534788	-1.1532888976	1.1949512437
C	-1.5315355343	0.40288748902	0.79179678682
C	-0.55754861285	1.3462417778	0.0092261442588
H	-1.3300141914	0.5136331542	1.853762702
H	-0.10580628823	2.0478251505	0.69899376915
C	-3.0282509572	0.67281279682	0.60449389175
H	-3.3496479273	0.55902276463	-0.42625996967
H	-3.2856201963	1.6774890713	0.9268151518
H	-3.612491025	-0.013880242803	1.2086911227
C	-1.2240553955	2.1992603966	-1.0822767436
H	-0.49670708487	2.8508451405	-1.5550274291
H	-1.9938239665	2.8367111057	-0.66109793392
H	-1.6797956306	1.5931841397	-1.860767686

Table S16. Coordinates of atoms in pentamethylcyclopentene of **Products E** optimized at the RHF/6-311+G** level

Total Energy (au): –392.0094325 (B3LYP/6-311+G**//RHF/6-311+G**)

atom	x	y	z
C	-0.7953714958	1.895365	0.91956775714
H	-0.80171342605	1.2005309699	1.7534339385
H	-0.14729688905	2.7244560941	1.1882565829
C	2.2686025893	1.5940201788	-0.13531367283
H	2.2103267797	2.1851642325	0.77537643052
H	2.2824640313	2.2938503448	-0.96842469347
H	3.2154421671	1.0699683539	-0.12562217219
C	2.2686136776	-1.5941447603	-0.13545101468
H	2.208886172	-2.1874810826	0.77366454808
H	3.2153002953	-1.0699201321	-0.12280388205
H	2.2840627076	-2.2919082848	-0.97022056416
C	-1.1190267233	-0.000078644956601	-0.86372302984
C	-0.31080902957	-1.2310749393	-0.37790767723
H	-1.0167343954	-0.00013845513196	-1.9466007634
H	-0.33168584596	-1.9994500525	-1.1511406177
C	-2.6161247651	-0.0000020693063458	-0.5623627403
H	-2.8327022884	0.00012743462082	0.50033612714
H	-3.0928959468	-0.87571169951	-0.99568477823
H	-3.0928307928	0.87564472678	-0.99588077136
C	-0.79547378001	-1.8951498223	0.91986318857
H	-0.14745780527	-2.7241879311	1.1888458966
H	-1.7982384423	-2.2958263155	0.80674824122
H	-0.80190864959	-1.200094172	1.7535465941
H	-1.7981342888	2.2960397874	0.80644387791
C	-0.3107749366	1.2309607211	-0.37805472017
H	-0.33158833205	1.9991774579	-1.151448013
C	1.093531033	-0.66336881233	-0.25269882958
C	1.0935383799	0.66323187177	-0.2527452426

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Single crystal of **3b** was also obtained from dichloromethane/ethanol. Although severe disorder was observed at the pyrene ring of **3b**, we could unambiguously check the bicyclo[3.3.0]octene skeleton.

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Chapter 2

Three-Step α-Acylation of (*E*)-Cinnamate Esters with Inversion of Stereochemistry through Formation and Cleavage of Carbon–Pentamethylcyclopentadienyl Bonds

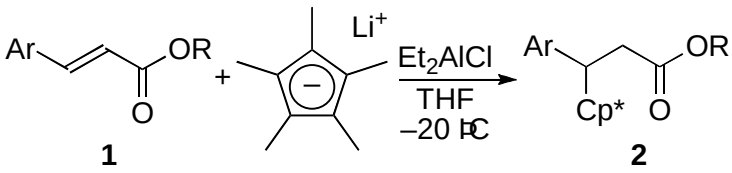
The reaction of cinnamate esters with lithium pentamethylcyclopentadienide in the presence of chlorodiethylaluminum provides the corresponding 1,4-adducts in high yield. The adducts undergo α-acylation reaction upon treatment with lithium diisopropylamide and acid chlorides. Removal of the pentamethylcyclopentadienyl group by the action of base affords α-acylcinnamate esters, in which the aryl and alkoxycarbonyl groups are in *cis* relationship.

Introduction

One can accomplish transformation of 2-alkenoate ester into 2-acylalkenoate ester by the following two methods. One is Morita–Baylis–Hillman reaction followed by oxidation of the resulting alcohol.[1] The other is a sequence of hydrogenation of 2-alkenoate ester, base-mediated α-acylation with acid chloride, and oxidation such as selenoxide elimination.[2] Here the author reports an alternative method. Conjugate addition of pentamethylcyclopentadienide ($Me_5C_5^-$, Cp^{*-}) to (*E*)-cinnamate esters yielded the corresponding adducts. The adducts sequentially underwent α-acylation and elimination of pentamethylcyclopentadiene (Cp*H) to yield (*Z*)-α-acylcinnamate esters. The overall transformation thus proceeded with inversion of configuration. The elimination step includes carbon–carbon bond cleavage of the Cp*–C bonds, which he has been focusing on.[3]

Results and Discussion

Treatment of methyl cinnamate (**1a**) with lithium pentamethylcyclopentadienide (Cp*Li) in the presence of chlorodiethylaluminum in THF at –20 ˚C provided the corresponding 1,4-adduct **2a** in 98% yield (eq. 1). Both electron-donating and withdrawing groups on the phenyl ring of **1** did not retard the addition reactions. Unfortunately, the addition reactions to methyl crotonate and butyl acrylate provided complex mixtures arising from oligomerizations of the unsaturated esters. The addition of lithium cyclopentadienide (CpLi), instead of Cp*Li, yielded a complex mixture under the otherwise identical reaction conditions. In the absence of chlorodiethylaluminum, the reaction did not proceed smoothly, and a half of **1** was recovered.

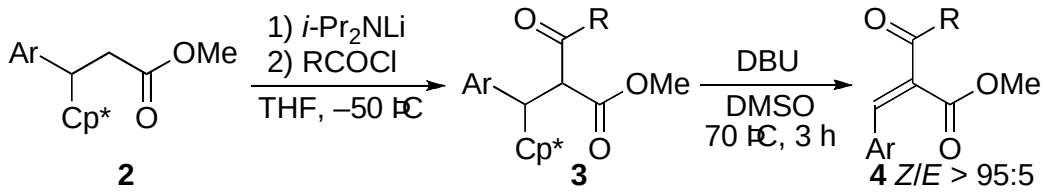


a: R = Me, Ar = Ph, 98%
b: R = Me, Ar = *p*-BrC_6H_4, 85%
c: R = Me, Ar = *p*-$MeOC_6H_4$, 81%
d: R = Et, Ar = *p*-NCC_6H_4, 95%
(1)

The adducts **2** were acylated with acid chlorides after deprotonation by lithium

diisopropylamide (Table 1, first step). The acylation provided products **3** as a single diastereomer whereas **3d** and **3g** were obtained as mixtures of two diastereomers in ratios of 94:6 (entries 4 and 7). The relative stereochemistry of the diastereomers could not be determined. The acylation reactions were performed at –50 ˚C, since higher temperatures induced the formation of **1** through liberation of Cp^{*-} from the corresponding lithium enolate of **2**. The acylation of **2** proceeded not only with aromatic acid chlorides but also with cyclohexanecarbonyl chloride (entry 3). Attempted acylations with pivaloyl chloride and with propanoyl chloride both resulted in the recovery of most of **2a**. The unsuccessful acylations are attributed to the steric reason of pivaloyl chloride and to the facile deprotonation reaction of propanoyl chloride with the enolate of **2a**. Acylation with electron-rich *p*-methoxybenzoyl chloride also resulted in failure.

Table 1. Transformation of the Cp* Adducts **2** to 2-Acylcinnamates **4**



entry	Ar	R	**3** /%	**4** /%
1	Ph (**2a**)	Ph	85, **3a**	93, **4a**
2	**2a**	*m*-$MeOC_6H_4$	83, **3b**	81, **4b**
3	**2a**	*c*-C_6H_{11}	82, **3c**	69, **4c**[a]
4	**2a**	*p*-MeC_6H_4	83, **3d**[b]	70, **4d**
5	**2a**	*o*-ClC_6H_4	83, **3e**	38, **4e**[c]
6	**2a**	*m*-ClC_6H_4	82, **3f**	78, **4f**
7	*p*-BrC_6H_4 (**2b**)	Ph	85, **3g**[b]	70, **4g**

[a] A 1:1 mixture of (*E*) and (*Z*) isomers. [b] A 94:6 mixture of diastereomers. [c] Initially a 45:55 mixture of (*E*) and (*Z*) isomers was obtained soon after aqueous workup. The isomeric mixture was quantitatively converted to the pure (*Z*) isomer (>95:5) upon standing the mixture overnight.

Treatment of **3** with 1,8-diazabicyclo[5.4.0]undecene (DBU) in dimethyl sulfoxide (DMSO) at 70 ˚C gave rise to the formation of the conjugated cinnamate skeleton, furnishing α-acylcinnamate esters **4** in good yields (Table 1, second step). It is worth noting that the aryl and methoxycarbonyl groups are on the same side of the double bond[4] except for **4c** and **4e**. The (*Z*) stereoselectivity of the reactions is quite similar to that of the Knoevenagel reaction.[4] The stereochemistry of **4** would thus be controlled at the elimination step. It is also probable that isomerization of the disfavored (*E*)-form into the thermodynamically stable (*Z*)-form occurred, which was indeed observed in the synthesis of **4e** (entry 5). The substituent at the *ortho* position of the aromatic acyl moiety interfered with the removal of the Cp* group (entry 5). A catalytic amount of DBU also induced the elimination reaction, albeit the efficiency was unsatisfactory. Treatment of **3a** with 0.30 equiv of DBU in DMSO at 70 ˚C for 6 h furnished **4a** in 68% yield.

Conclusion

The author have developed a three-step α-acylation of (*E*)-cinnamate ester with inversion of configuration. The transformation takes advantage of the facile carbon–Cp* bond cleavage.

Experimental Section

General Procedure for Nucleophilic Addition of Cp*Li to α,β-Unsaturated Ester

A solution of butyllithium in hexane (1.67 M, 12.0 mL, 20 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (3.3 mL, 21 mmol) in THF (100 mL) at –20 ˚C. The mixture was stirred for 30 min at the same temperature to provide a white suspension of lithium pentamethylcyclopentadienide. Chlorodiethylaluminum (2.5 mL, 21 mmol) was added to the resulting mixture, and the reaction mixture was stirred for 30 min at –20 ˚C. After an addition of a solution of **1a** (1.62 g, 10 mmol) in THF (10 mL), the mixture was stirred for an additional 1 h at –20 ˚C. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane/ethyl acetate = 30:1) to afford **2a** (2.92 g, 9.8 mmol, 98%).

General Procedure for Acylation of 1,4-Adduct

A solution of butyllithium in hexane (1.55 M, 0.71 mL, 1.1 mmol) was added to a solution of diisopropylamine (0.17 mL, 1.2 mmol) in THF (10 mL) at 0 ˚C. The mixture was stirred for 30 min at the same temperature. The reaction mixture was cooled to –50 ˚C. A THF (1 mL) solution of ester **2a** (298 mg, 1.0 mmol) was added to the resulting mixture, and the reaction mixture was stirred for 5 h. Benzoyl chloride (0.14 mL, 1.2 mmol) was added to the reaction mixture, and the mixture was stirred for 2 h at –50 ˚C. After being stirred for 2 h, the reaction was quenched with water. The mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried and concentrated. The oil obtained was chromatographed on silica gel (hexane/ethyl acetate = 10:1) to afford **3a** (342 mg, 0.85 mmol, 85%).

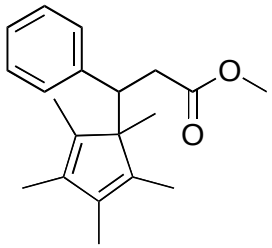
Typical Procedure for Elimination of Cp*H

1,8-Diazabicyclo[5.4.0]undecene (0.050 mL, 0.36 mmol) was added to a solution of **3a** in dimethyl sulfoxide (6.0 mL). The reaction mixture was warmed to 70 ˚C and the mixture was stirred for 3 h. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic parts were washed with brine, dried and concentrated. Chromatographic purification on silica gel (Wakogel C-200, hexane/ethyl acetate = 5:1) afforded **4a** (62.4 mg, 0.28 mmol, 93%). The NMR spectra of **4a** were identical to those reported in ref. 4.

Characterization Data

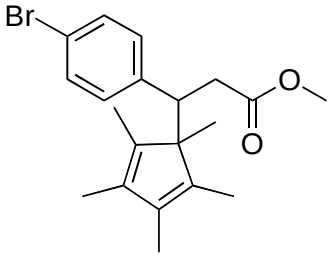
The spectral data of **4a** are found in the literature.[4]

Methyl 3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-3-phenylpropanoate (2a)



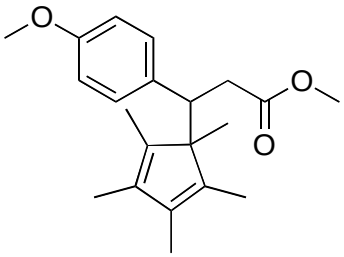
IR (nujol) 1743 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.92 (s, 3H), 1.55 (s, 6H), 1.64 (bs, 3H), 1.82 (s, 3H), 2.44 (dd, *J* = 2.1, 9.6 Hz, 1H), 2.75 (dd, *J* = 6.9, 9.6 Hz, 1H), 3.15 (s, 3H), 5.54 (dd, *J* = 2.1, 6.9 Hz, 1H), 7.01–7.11 (m, 5H); ^{13}C NMR (C_6D_6) δ 10.89, 11.04, 11.07, 11.88, 20.30, 34.79, 46.66, 50.94, 58.88, 126.72, 127.55 (× 2), 128.29, 129.52 (× 2), 131.48, 135.72, 140.31, 140.71, 172.87. Found: C, 80.50; H, 8.78%. Calcd for $C_{20}H_{26}O_2$: C, 80.80; H, 8.97%. m.p. 47–49 ˚C.

Methyl 3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-3-(4-bromophenyl)propanoate (2b)



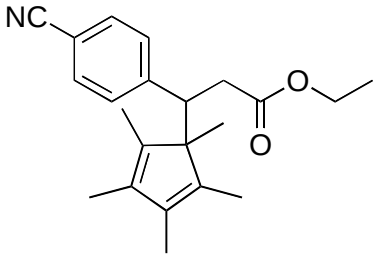
IR (nujol) 1733 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (s, 3H), 1.55 (s, 3H), 1.60 (s, 3H), 1.70 (s, 3H), 1.86 (s, 3H), 2.43 (dd, *J* = 3.5, 16 Hz, 1H), 2.56 (dd, *J* = 11.5, 16 Hz, 1H), 3.24 (dd, *J* = 3.5, 11.5 Hz, 1H), 3.47 (s, 3H), 6.95–7.00 (m, 2H), 7.27–7.32 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.82, 11.00, 11.24, 11.58, 19.88, 34.50, 45.90, 51.49, 58.17, 120.09, 130.23 (× 2), 130.43 (× 2), 135.51, 136.14, 139.18, 139.39, 139.61, 173.36. Found: C, 63.91; H, 6.79%. Calcd for $C_{20}H_{25}BrO_2$: C, 63.66; H, 6.68%. m.p. 69–72 ˚C.

Methyl 3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-3-(4-methoxyphenyl)propanoate (2c)



IR (neat) 2956, 1739, 1611, 1514, 1436, 1249 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (s, 3H), 1.55 (s, 3H), 1.64 (s, 3H), 1.72 (s, 3H), 1.86 (s, 3H), 2.33 (dd, *J* = 3.6, 15.9 Hz, 1H), 2.55 (dd, *J* = 11.7, 15.9 Hz, 1H), 3.23 (dd, *J* = 3.6, 11.7 Hz, 1H), 3.46 (s, 3H), 3.77 (s, 3H), 6.71–6.78 (m, 2H), 6.71–7.19 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.71, 10.78, 10.87, 11.66, 19.31, 34.36, 45.25, 51.17, 54.85, 58.43, 112.40 (× 2), 129.82 (× 2), 132.02, 135.15, 135.30, 139.73, 139.75, 157.83, 173.54. HRMS Found: 328.2042. Calcd for $C_{21}H_{28}O_3$: 328.2038.

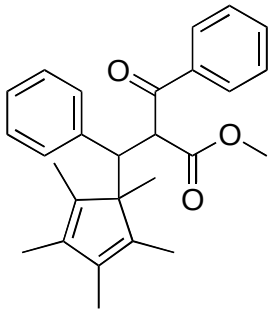
Ethyl 3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-3-(4-cyanophenyl)propanoate (2d)



IR (neat) 2965, 2925, 2228, 1733, 1445, 1372 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 3H), 1.04 (t, *J* = 7.2 Hz, 3H), 1.53 (s, 3H), 1.58 (s, 3H), 1.67 (s, 3H), 1.90 (s, 3H), 2.50–2.68 (m, 2H), 3.26–3.38 (m, 1H), 3.82–4.00 (m, 2H), 7.18–7.22 (m, 2H), 7.37–7.50 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.52,

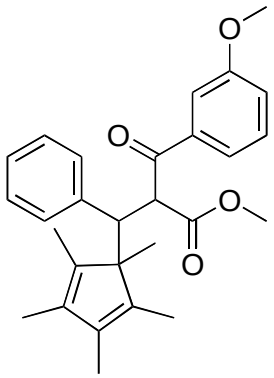
10.76, 11.12, 11.49, 13.80, 19.42, 34.52, 46.71, 57.95, 60.11, 109.83, 118.89, 129.00 (× 2), 130.01 (× 2), 135.41, 136.59, 138.35, 139.25, 146.16, 172.28. HRMS Found: 337.2045. Calcd for $C_{22}H_{27}NO_2$: 337.2042.

Methyl 2-benzoyl-3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-3-phenylpropanoate (3a)



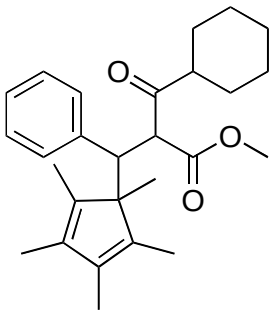
IR (nujol) 1736, 1686 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.79 (s, 3H), 1.62 (s, 3H), 1.66 (s, 3H), 1.81 (s, 3H), 2.02 (s, 3H), 3.62 (s, 3H), 3.98 (d, J = 6.9 Hz, 1H), 5.11 (d, J = 6.9 Hz, 1H), 6.94–7.02 (m, 5H), 7.34–7.38 (m, 2H), 7.46–7.50 (m, 1H), 7.76–7.80 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.85, 11.21, 11.76, 12.18, 21.00, 49.65, 52.32, 55.52, 58.46, 125.96, 126.97 (× 2), 128.10 (× 2), 128.23, (× 2), 129.11 (× 2), 132.78, 135.73, 135.82, 137.12, 138.92, 139.48, 139.93, 168.23, 193.98. Found: C, 80.30; H, 7.50%. Calcd for $C_{27}H_{30}O_3$: C, 80.56; H, 7.51%. m.p. 135–136 ˚C.

Methyl 2-(3-methoxybenzoyl)-3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-3-phenylpropanoate (3b)



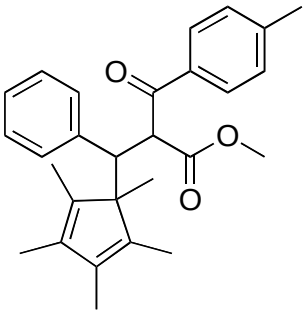
IR (nujol) 1733, 1684, 1597 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.95 (s, 3H), 1.58 (s, 3H), 1.62 (bs, 3H), 1.86 (s, 3H), 2.11 (s, 3H), 3.06 (s, 3H), 3.23 (s, 3H), 4.41 (d, *J* = 11.1 Hz, 1H), 5.46 (d, *J* = 11.1 Hz, 1H), 6.76–6.80 (m, 1H), 6.82–7.30 (m, 6H), 7.49–7.53 (m, 1H), 7.78–7.84 (m, 1H); ^{13}C NMR (C_6D_6) δ 10.90, 11.23, 11.97, 12.19, 21.30, 49.89, 51.94, 54.58, 56.27, 59.00, 112.50, 120.33, 121.24, 126.50, 127.26 (× 2), 129.69 (× 2), 129.82, 136.03, 136.20, 139.29, 140.03, 140.27, 140.59, 160.28, 168.64, 193.25. HRMS Found: 432.2302. Calcd for $C_{28}H_{32}O_4$: 432.2301. m.p. 118–122 ˚C.

Methyl 2-cyclohexanecarbonyl-3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-3-phenylpropanoate (3c)



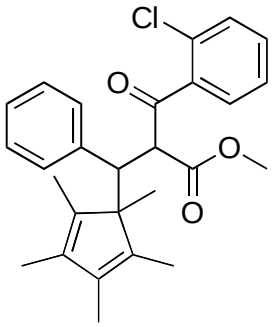
IR (neat) 2932, 2855, 1750, 1714, 1451 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.92 (s, 3H), 0.93–1.50 (m, 13H), 1.59 (s, 3H), 1.78 (s, 3H), 2.07 (s, 3H), 2.40–2.46 (m, 1H), 3.32 (s, 3H), 4.12 (d, *J* = 11.5 Hz, 1H), 4.51 (d, *J* = 11.5 Hz, 1H), 6.93–7.14 (m, 5H); ^{13}C NMR (C_6D_6) δ 10.99, 11.33, 12.03, 12.48, 20.91, 25.95, 25.98, 26.09, 28.52, 29.83, 50.10, 51.26, 52.03, 59.23, 61.61, 126.98 (× 2), 127.48 (× 2), 130.30, 135.85, 136,73, 139.62, 140.29, 140.61, 169.56, 206.43. HRMS Found: 408.2669. Calcd for $C_{27}H_{36}O_3$: 408.2664.

Methyl 2-(4-methylbenzoyl)-3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-3-phenylpropanoate (3d)



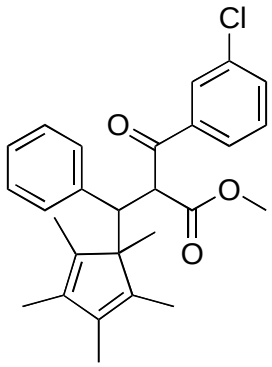
IR (neat) 1729, 1674 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.96 (s, 3H), 1.59 (s, 3H), 1.61 (bs, 3H), 1.85 (s, 3H), 1.89 (s, 3H), 2.13 (s, 3H), 3.23 (s, 3H), 4.42 (d, *J* = 11.1 Hz, 1H), 5.45 (d, *J* = 11.1 Hz, 1H), 6.74-7.20 (m, 7H), 7.96–8.02 (m, 2H); ^{13}C NMR (C_6D_6) δ 10.93, 11.23, 11.96, 12.23, 21.18, 21.34, 49.75, 51.84, 56.07, 59.02, 126.47 (× 2), 127.21 (× 2), 128.94 (× 2), 129.43 (× 2), 129.81, 135.45, 136.03, 136.14, 140.08, 140.29, 140.67, 143.70, 168.74, 192.80. HRMS Found: 416.2354. Calcd for $C_{28}H_{32}O_3$: 416.2351.

Methyl 2-(2-chlorobenzoyl)-3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl-3-phenylpropanoate (3e)



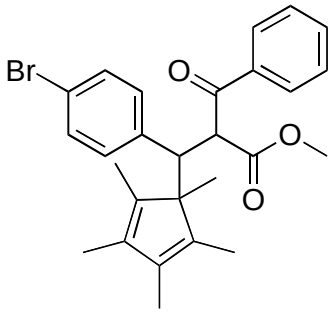
IR (neat) 2926, 2857, 1732, 1699, 1436, 1251, 1151, 1065, 967 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.96 (s, 3H), 1.46 (s, 3H), 1.57 (s, 3H), 1.80 (s, 3H), 2.10 (s, 3H), 3.31 (s, 3H), 4.23 (d, *J* = 6.9 Hz, 1H), 5.30 (d, *J* = 6.9 Hz, 1H), 6.54–6.64 (m, 2H), 6.85–7.34 (m, 7H); ^{13}C NMR (C_6D_6) δ 10.79, 11.17, 11.86, 12.19, 21.04, 50.97, 51.99, 59.01, 59.86, 126.51, 126.74, 127.35 (× 2), 128.29, 129.70 (× 2), 130.65, 131.71, 131.78, 135.66, 136.47, 139.09, 139.24, 140.11, 140.51, 168.57, 194.87. HRMS Found: 436.1804. Calcd for $C_{27}H_{29}ClO_3$: 436.1805.

Methyl 2-(3-chlorobenzoyl)-3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)-3-phenylpropanoate (3f)



IR (nujol) 1742, 1687 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.92 (s, 3H), 1.54 (bs, 3H), 1.58 (s, 3H), 1.82 (s, 3H), 2.06 (s, 3H), 3.20 (s, 3H), 4.32 (d, *J* = 11.1 Hz, 1H), 5.27 (d, *J* = 11.1 Hz, 1H), 6.56–6.65 (m, 1H), 6.82–7.14 (m, 6H), 7.72–7.78 (m, 1H), 8.02 (bs, 1H); ^{13}C NMR (C_6D_6) δ 10.88, 11.20, 11.90, 12.16, 21.22, 49.95, 52.03, 56.61, 58.92, 126.60, 126.67, 127.32 (× 2), 128.61, 129.78 (× 2), 130.01, 132.85, 135.09, 136.20, 136.34, 139.44, 139.58, 140.13, 140.44, 168.33, 192.37. Found: C, 73.93; H, 6.74%. Calcd for $C_{27}H_{29}ClO_3$: C, 74.21; H, 6.69%. m.p. 131–133 ˚C.

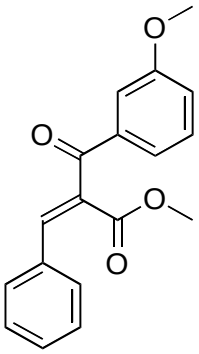
Methyl 2-benzoyl-3-(4-bromophenyl)-3-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl)propanoate (3g)



IR (nujol) 1740, 1695 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.87 (s, 3H), 1.52 (s, 3H), 1.55 (bs, 3H), 1.74 (s, 3H), 2.04 (s, 3H), 3.18 (s, 3H), 4.26 (d, *J* = 11.1 Hz, 1H), 5.32 (d, *J* = 11.1 Hz, 1H), 6.80–7.10 (m, 7H), 7.95–8.02 (m, 2H); ^{13}C NMR (C_6D_6) δ 10.81, 11.14, 11.96, 12.04, 20.94, 49.35, 51.98, 55.88, 58.74, 120.43, 128.66 (× 2), 128.77 (× 2), 130.26 (× 2), 131.32, 133.17 (× 2), 136.13,

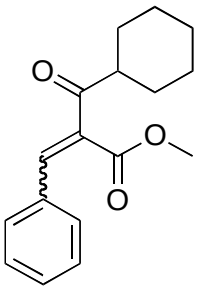
136.72, 137.63, 139.00, 140.00, 140.14, 168.46, 193.14. Found: C, 67.10; H, 6.12%. Calcd for $C_{27}H_{29}BrO_3$: C, 67.36; H, 6.07%. m.p. 105–110 ˚C.

Methyl (*Z*)–2-(3-methoxybenzoyl)-3-phenylpropenoate (4b)



IR (neat) 1717, 1668, 1622, 1596, 1436, 1324, 1201 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.75 (s, 3H), 3.82 (s, 3H), 7.07–7.55 (m, 9H), 7.97 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 52.57, 55.36, 112.50, 120.79, 122.27, 128.75 (× 2), 129.86, 130.16 (× 2), 130.40, 130.71, 132.65, 137.13, 142.77, 159.93, 165.39, 195.32. Found: C, 72.90; H, 5.64%. Calcd for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44%.

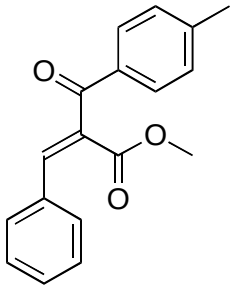
Methyl 2-cyclohexanecarbonyl-3-phenylpropenoate (4c, 1:1 mixture of stereoisomers)



IR (neat) 2931, 2855, 1732, 1718, 1700, 1695, 1616, 1576, 1448, 1436, 1256, 1201 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02–1.96 (m, 10H), 2.32–2.45 (m, 1 × 0.5H), 2.82–2.96 (m, 1 × 0.5H), 3.820 (s, 3 × 0.5H), 3.824 (s, 3 × 0.5H), 7.34–7.46 (m, 5H), 7.58 (s, 1 × 0.5H), 7.77 (s, 1 × 0.5H); ^{13}C NMR ($CDCl_3$) δ 25.57 (× 2), 25.65 (× 3), 25.74, 28.22 (× 2), 29.14 (× 2), 46.22, 51.33, 52.47, 52.50, 128.76 (× 2), 128.84 (× 2), 129.37 (× 2), 129.76 (× 2), 130.37, 130.55, 133.10 (× 2), 133.23, 133.47, 140.76, 141.39, 165.34, 168.56, 200.28, 208.66. Found: C, 75.12; H, 7.55%.

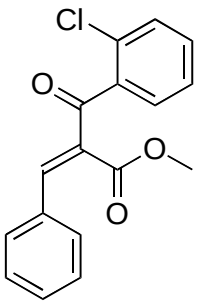
Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40%.

Methyl (*Z*)-2-(4-methylbenzoyl)-3-phenylpropenoate (4d)



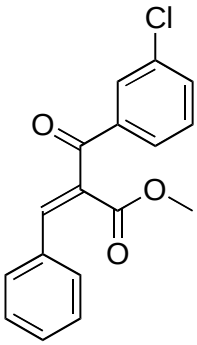
IR (nujol) 1695, 1652, 1603, 1572 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.37 (s, 3H), 3.74 (s, 3H), 7.15–7.42 (m, 7H), 7.82–7.90 (m, 2H), 7.96 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.70, 52.51, 128.69 (× 2), 129.30 (× 2), 129.56 (× 2), 130.15 (× 2), 130.29, 130.86, 132.70, 133.42, 142.49, 145.04, 165.51, 195.13. Found: C, 76.82; H, 5.84%. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75%. m.p. 103–105 ˚C.

Methyl (*Z*)-2–(2-chlorobenzoyl)-3-phenylpropenoate (4e)



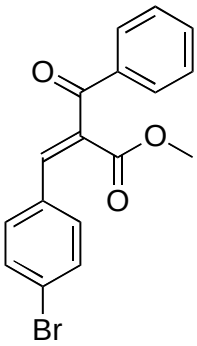
IR (nujol) 1732, 1668, 1587 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.83 (s, 3H), 7.26–7.52 (m, 8H), 7.81–7.85 (m, 1H), 7.97 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 52.59, 126.76, 128.68 (× 2), 130.02 (× 2), 130.44, 131.48, 131.88, 132.44, 132.77, 133.43, 133.82, 135.34, 143.25, 165.29, 193.57. Found: C, 67.55; H, 4.62%. Calcd for $C_{17}H_{13}ClO_3$: C, 67,89; H, 4.36%. m.p. 79–82 ˚C.

Methyl (*Z*)-2-(3-chlorobenzoyl)-3-phenylpropenoate (4f)



IR (neat) 1725, 1678, 1623, 1434, 1284, 1223, 1201, 1073 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.77 (s, 3H), 7.24–7.38 (m, 6H), 7.51–7.54 (m, 1H), 7.77–7.80 (m, 1H), 7.93–7.95 (m, 1H), 8.00 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 52.65, 127.36, 128.85 (× 2), 128.88, 130.04, (× 2), 130.12, 130.19, 130.63, 132.42, 133.89, 135.17, 137.36, 143.39, 165.11, 194.23. Found: C, 67.93; H, 4.63%. Calcd for $C_{17}H_{13}ClO_3$: C, 67.89; H, 4.36%.

Methyl (*Z*)-2-benzoyl-3-(4-bromophenyl)propenoate (4g)



IR (neat) 2952, 1722, 1674, 1622, 1587, 1489, 1449, 1435 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.75 (s, 3H), 7.18–7.58 (m, 7H), 7.90 (s, 1H), 7.90–7.94 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 52.69, 124.97, 128.94 (× 2), 129.14 (× 2), 131.45 (× 2), 131.57, 132.04 (× 2), 134.21, 135.60, 141.32 (× 2), 165.21, 195.24. Found: C, 59.11; H, 3.91%. Calcd for $C_{17}H_{13}BrO_3$: C, 59.15; H, 3.80%.

References and Notes

(1) (a) N. J. Lawrence, J. P. Crump, A. T. McGown, J. A. Hadfield, *Tetrahedron Lett.* **2001**, *42*, 3939. (b) H. M. R. Hoffmann, A. Gassner, U. Eggert, *Chem. Ber.* **1991**, *124*, 2475.

(2) (a) S. Danishefsky, S. Chackalamannil, B.-J. Uang, *J. Org. Chem.* **1982**, *47*, 2231. (b) T. R. Hoye, A. J. Caruso, A. S. Magee, *J. Org. Chem.* **1982**, *47*, 4152. (c) K. C. Nicolaou, T. Montagnon, P. S. Baran, *Angew. Chem. Int. Ed.* **2002**, *41*, 993.

(3) (a) K. Yagi, H. Yorimitsu, K. Oshima, *Tetrahedron Lett.* **2005**, *46*, 4831. (b) M. Uemura, H. Yorimitsu, K. Oshima, *Tetrahedron Lett.* **2006**, *47*, 163. (c) M. Uemura, K. Yagi, M. Iwasaki, K. Nomura, H. Yorimitsu, K. Oshima, *Tetrahedron* **2006**, *62*, 3523.

(4) The stereochemistry of **4a** was confirmed according to the literature: R. Tanikaga, N. Konya, K. Hamamura, A. Kaji, *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3211.

Chapter 3

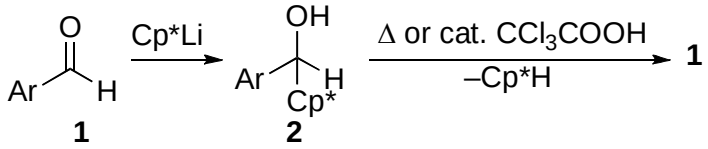
Synthesis of β,γ-Unsaturated Ketones from Acid Chlorides through Carbon–Pentamethylcyclopentadienyl Bond Formation and Cleavage

Reaction of acid chlorides with lithium pentamethylcyclopentadienide afforded the corresponding pentamethylcyclopentadienyl ketones in high yields. These ketones were treated with an allylaluminum reagent to form the corresponding 3-butenyl alcohols. Removal of pentamethylcyclopentadiene upon heating or treatment with a catalytic amount of trichloroacetic acid yielded the corresponding β,γ-unsaturated ketones in good yields..

Introduction

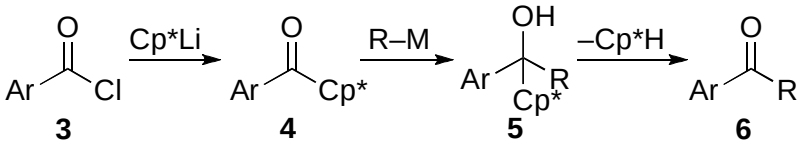
The author has been exploring applications of pentamethylcyclopentadiene (Me_5C_5H, Cp*H) as a reagent in organic synthesis and developing new reactions.[1] He has reported that Cp*Li reacted with aromatic aldehydes **1** to provide the corresponding secondary alcohols **2** in excellent yields. The secondary alcohols easily returned to the parent aldehydes and Cp*H under thermal or acidic conditions (Scheme 1).[1a,1c]

Scheme 1.



Thus, the author expected that alcohol **5**, which is prepared from acid chloride **3** *via* **4**, would smoothly transform to ketone **6** by removal of Cp*H (Scheme 2). Using this approach, he planned to synthesize β,γ-unsaturated ketones.[2] Synthesis of β,γ-unsaturated ketones is often complicated, since β,γ-unsaturated ketones easily isomerize to α,β-unsaturated ketones under acidic or basic conditions. Here, he reports[1e] a new method to synthesize β,γ-unsaturated ketones from acid chlorides in three steps as shown in Scheme 2, wherein R–M is an allylmetal reagent.

Scheme 2.



Results and Discussion

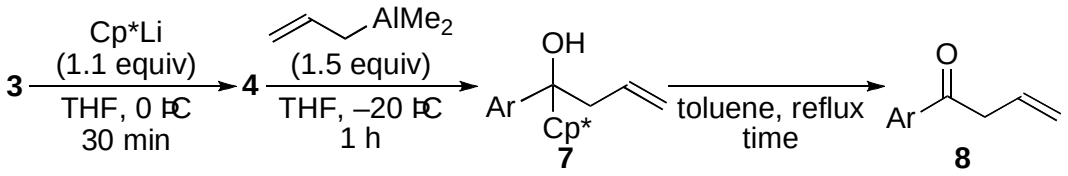
Treatment of Cp*Li (1.1 equiv) with benzoyl chloride (**3a**) in THF at 0 ˚C for 30 min afforded pentamethylcyclopentadienyl phenyl ketone (**4a**) in excellent yield (Table 1, entry 1).

A variety of aromatic acid chlorides **3** were subjected to the nucleophilic addition reaction of Cp*Li to afford aryl pentamethylcyclopentadienyl ketones **4**. Acid chlorides **3** bearing an electron-withdrawing group (entry 2) or an electron-donating group (entry 3) afforded **4** in high yields. Bromine (entry 4) and chlorine (entry 5) on the aromatic ring did not interfere with the reaction. Reaction of *ortho*-substituted **3** also proceeded smoothly (entries 6 and 7). Heteroaromatic acid chlorides, such as thiophene- (entry 8) and furancarbonyl chloride (entry 9), could be used in this reaction.

Ketone **4a** was treated with 1.5 equiv of an allylaluminum reagent, which was prepared from allylmagnesium bromide and dimethylaluminum chloride, at –20 ˚C for 1 h to afford the homoallyl alcohol **7a** in 98% yield.[3] In contrast, the reaction of benzoyl chloride (**3a**), instead of **4a**, with the allylaluminum reagent gave diallylated alcohol **9** (Scheme 3). In addition, when **4a** was treated with allylmagnesium chloride, instead of the allylaluminum reagent, **9** was obtained exclusively (Scheme 4). Nucleophilic addition of allylmagnesium chloride to ketone **8a**, which was generated by *in situ* elimination of Cp*MgCl from alkoxide **10**, should give **9**.

At room temperature, Cp*H was liberated from **7a** very slowly to give allyl phenyl ketone (**8a**). Then he found that heating crude **7a** in toluene at reflux for 1 h provided **8a** in good yield (Table 1, entry 1). The reaction of ketones **4** having trifluoromethyl (entry 2), methoxy (entry 3), bromo (entry 4) or chloro moieties (entry 5) also afforded **8** in moderate to good yields. Unfortunately, *ortho*-substituted **4f** and **4g** (entries 6 and 7) did not undergo the nucleophilic addition reaction with the allylaluminum reagent even at 0 ˚C. Allylation of **4f** and **4g** took place at room temperature. However, similar diallylation as shown in Scheme 3 occurred. Although the reaction of 2-furyl pentamethylcyopentadienyl ketone (**4i**) with the allylaluminum reagent afforded **7i** in high yield, heating **7i** provided a complex mixture (entry 9).

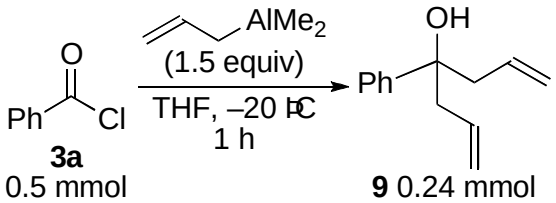
Table 1. Synthesis of Allyl Aryl Ketones



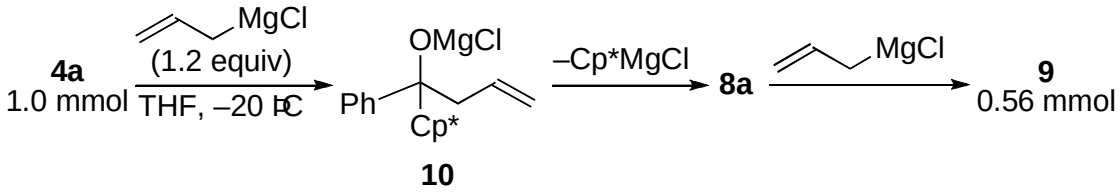
entry	Ar	**4** /%	time	**8** /%[a,b]
1	Ph (**a**)	96	1 h	70
2	*p*-$CF_3C_6H_4$ (**b**)	92	1 h 15 min	68
3	*p*-$MeOC_6H_4$ (**c**)	85	1 h	90
4	*p*-BrC_6H_4 (**d**)	93	1 h 15 min	80
5	*m*-ClC_6H_4 (**e**)	98	1 h 30 min	66
6	*o*-MeC_6H_4 (**f**)	96	–	–
7	*o*-IC_6H_4 (**g**)	78	–	–
8	2-Thienyl (**h**)	91	30 min	65
9	2-Furyl (**i**)	91	45 min	8[c]

[a] Isolated yield based on **4**. [b] Trace amounts (< 0~7%) of α,β-unsaturated ketones were detected. [c] NMR yield.

Scheme 3.

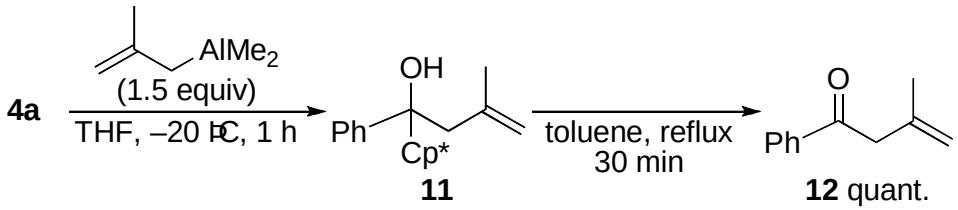


Scheme 4.



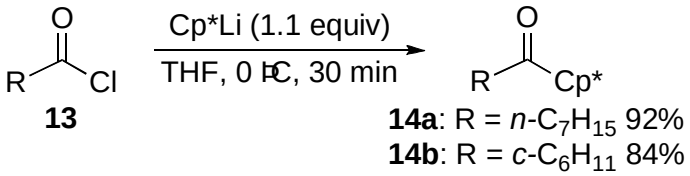
2-Methyl-2-propenyl (here after named methallyl) phenyl ketone (**12**) was also synthesized in a similar manner from **4a** and a methallylaluminum reagent in quantitative yield (Scheme 5). Unfortunately, nucleophilic addition reactions of 2-butenyl- and 2-methyl-2-butenylaluminum reagents with **4a** resulted in recovery of **4a** even at 0 ˚C.

Scheme 5.

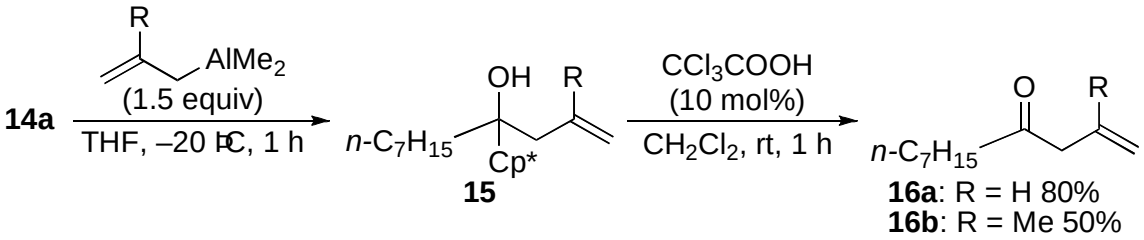


Preparation of aliphatic pentamethylcyclopentadienyl ketone **14** was performed in a similar fashion (Scheme 6). Although allylation and methallylation of heptyl ketone **14a** proceeded smoothly to provide alcohols **15** (Scheme 7), cyclohexyl ketone **14b** resisted the allylation. In contrast to aromatic alcohols **7**, alcohols **15** were stable at reflux in toluene (110 ˚C). However, **15** were unstable under acidic conditions and were transformed into the β,γ-unsaturated ketones effectively. Treatment of **15** with 10 mol% of trichloroacetic acid in dichloromethane at room temperature for 1 h provided the corresponding ketones **16** in moderate to good yields (Scheme 7).

Scheme 6.

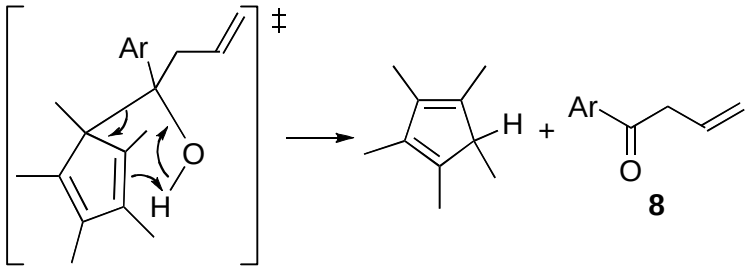


Scheme 7.

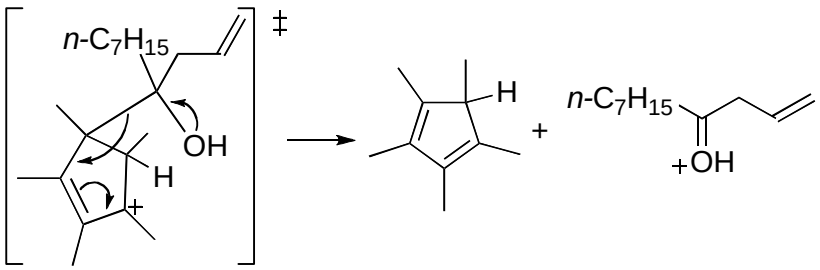


The proposed reaction mechanisms of the removal of Cp*H are shown in Scheme 8 and 9.[1a,1c] A retro-carbonyl-ene mechanism could be used to rationalize the fragmentation reaction under thermal conditions (Scheme 8). Protonation at the Cp* group could facilitate carbon–carbon bond cleavage under acidic conditions (Scheme 9).

Scheme 8.



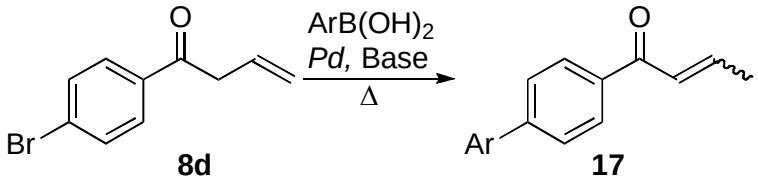
Scheme 9.



A typical Suzuki–Miyaura cross-coupling reaction needs a strong base and high temperature.[4] If **8d** was used as a substrate of Suzuki–Miyaura cross-coupling reaction, an

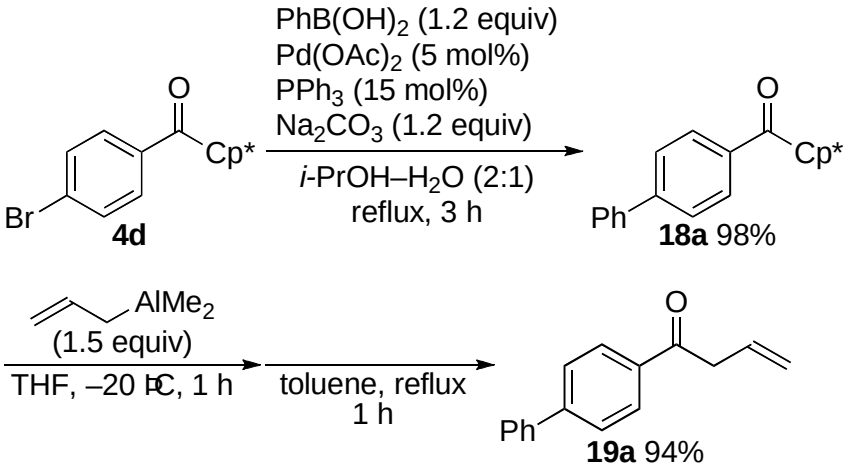
α,β-unsaturated coupling product would be obtained (Scheme 10).

Scheme 10.

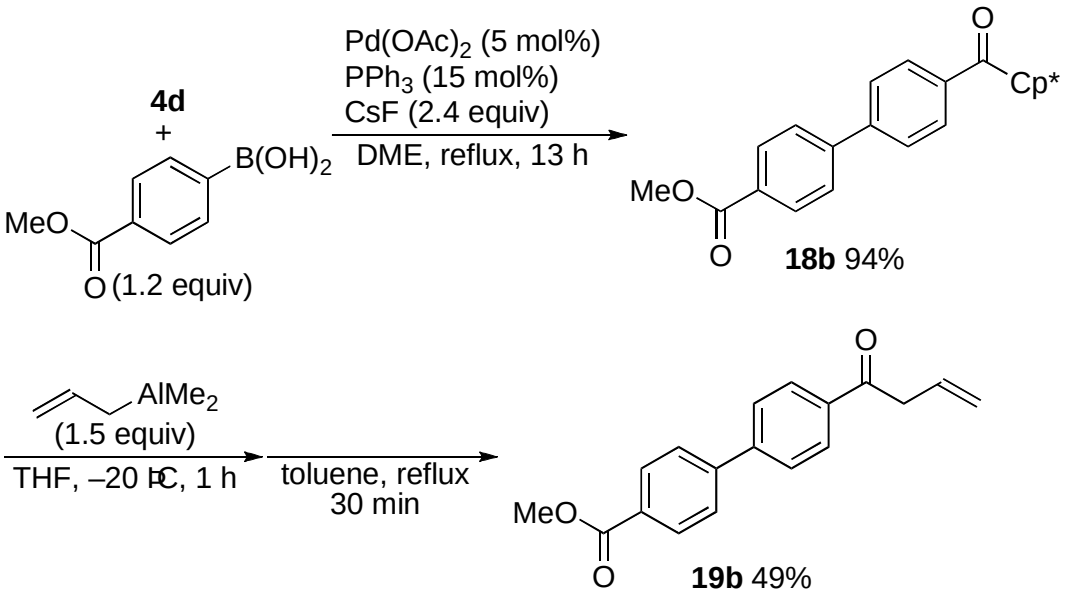


Thus, he examined an alternative method to prepare β,γ-unsaturated coupling product **19**. Aryl halides that have a pentamethylcyclopentadienylcarbonyl part were used in the cross-coupling reaction, and then the coupling products were transformed to β,γ-unsaturated ketones upon treatment with an allylaluminum reagent, followed by heating. Treatment of **4d** and **4e** with arylboronic acid under palladium catalysis yielded biaryls **18** in good yields (Scheme 11–13). Ketones **18** were converted into the corresponding β,γ-unsaturated ketones **19** under similar conditions shown in Table 1. Fortunately, an ester moiety survived during the nucleophilic addition reaction of the allylaluminum reagent (Scheme 12)

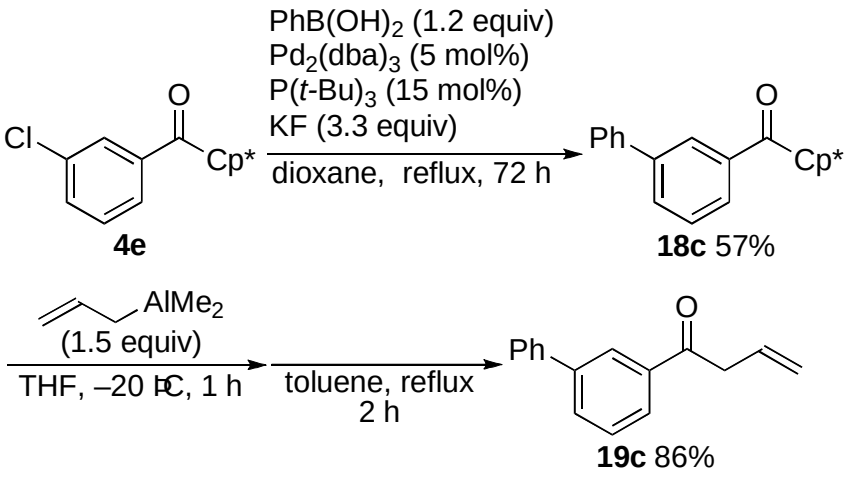
Scheme 11.



Scheme 12.

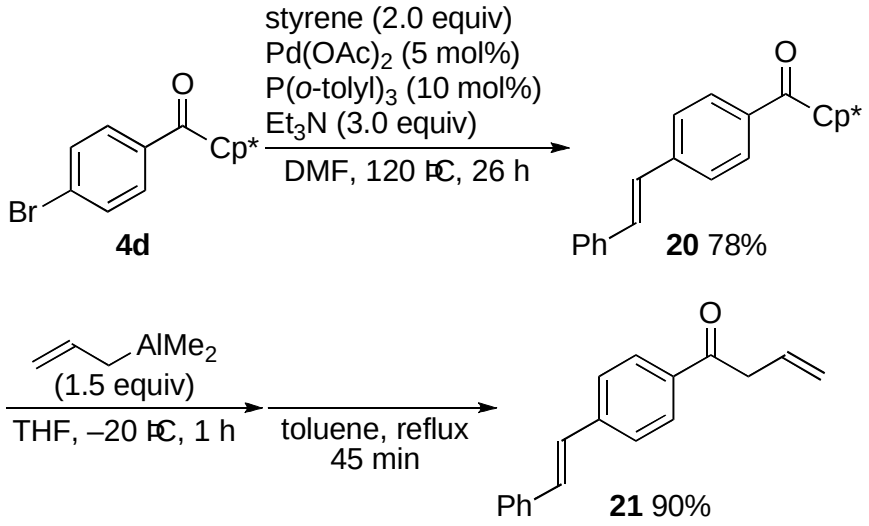


Scheme 13.



This approach could be also applicable to the Mizoroki–Heck reaction, which requires basic conditions (Scheme 14).[5]

Scheme 14.


styrene (2.0 equiv)
Pd(OAc)2 (5 mol%)
P(o-tolyl)3 (10 mol%)
Et3N (3.0 equiv)
DMF, 120 °C, 26 h
O
Cp*
Br
4d
Ph
20 78%
AlMe2
(1.5 equiv)
THF, –20 °C, 1 h
toluene, reflux
45 min
21 90%

Experimental Section

General Procedure for Nucleophilic Addition Reaction of Cp*Li to Aromatic Acid Chlorides (Table 1)

A solution of butyllithium in hexane (1.60 M, 1.38 mL, 2.20 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.38 mL, 2.40 mmol) in THF (20 mL) at 0 ˚C. The mixture was stirred for 30 min at the same temperature to generate a white suspension of lithium pentamethylcyclopentadienide. After an addition of *m*-chlorobenzoyl chloride (350 mg, 2.00 mmol) in THF (1 mL), the mixture was stirred for an additional 30 min at 0 ˚C. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane/ethyl acetate = 40:1) to afford 3-chlorophenyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (**4e**) (536 mg, 1.95 mmol, 98%).

General Procedure for Nucleophilic Addition Reaction of Allylaluminum Reagent to Aromatic Ketones and Thermal Cleavage Reaction (Table 1)

A solution of dimethylaluminum chloride in hexane (1.04 M, 0.72 mL, 0.75 mmol) was added to a solution of allylmagnesium bromide in diethyl ether (0.87 M, 0.86 mL, 0.75 mmol) at –20 ˚C. After the mixture was stirred for 10 min at the same temperature, **4e** (137 mg, 0.50 mmol) in THF (2.5 mL) was added to the reaction mixture. The mixture was stirred for 1 h at –20 ˚C. The reaction mixture was quenched with dilute aqueous HCl. The mixture was extracted with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give a crude oil. The oil was filtered through a short pad of silica gel (ethyl acetate), and the filtrate was concentrated *in vacuo*. The oil was used for the next step without further purification. The resulting oil was dissolved in toluene (5 mL) and heated at reflux for 1.5 h. The mixture was concentrated and purified by chromatography on silica gel (Wakogel C-200, hexane/ethyl acetate = 20:1) and GPC (toluene) to afford allyl 3-chlorophenyl

ketone (**8e**) (59.1 mg, 0.33 mmol, 66%).

The crude **7a** could be isolated by chromatography on silica gel (Silica Gel 60N, hexane/ethyl acetate = 10:1) in 98% yield (139 mg, 0.49 mmol).

General Procedure for Nucleophilic Addition Reaction of Allylic Aluminum Reagent to Aliphatic Ketones and Acid-Induced Cleavage Reaction (Scheme 7)

A solution of dimethylaluminum chloride in hexane (1.04 M, 0.72 mL, 0.75 mmol) was added to a solution of 2-methyl-2-propenylmagnesium chloride in THF (0.89 M, 0.84 mL, 0.75 mmol) at –20 ˚C. After the suspension was stirred for 10 min at –20 ˚C, a solution of **14a** (131 mg, 0.50 mmol) in THF (2.5 mL) was added to the mixture. The whole mixture was stirred for 1 h at –20 ˚C. Dilute aqueous HCl was added to quench the reaction. Extraction with ethyl acetate and evaporation under reduced pressure afforded the crude oil. The oil was passed through a pad of silica gel with ethyl acetate, and the filtrate was concentrated *in vacuo*. A solution of trichloroacetic acid in dichloromethane (0.1 M, 0.50 mL, 0.05 mmol) was added to a solution of the resulting oil in dichloromethane (3.3 mL) at room temperature. The mixture was stirred for 1 h at room temperature. After the reaction was quenched with saturated aqueous $NaHCO_3$, the mixture was extracted with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Silica gel column chromatography (Wakogel C-200, hexane/ethyl acetate = 20:1) and GPC purification (toluene) provided heptyl 2-methyl-2-propenyl ketone (**16b**) (45.5 mg, 0.25 mmol, 50%).

Synthesis of 4-Biphenylyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (18a)

A mixture of **4d** (638 mg, 2.00 mmol), phenylboronic acid (293 mg, 2.40 mmol), $Pd(OAc)_2$ (22.4 mg, 0.10 mmol), triphenylphosphine (78.7 mg, 0.30 mmol), and Na_2CO_3 (254 mg, 2.40 mmol) in isopropyl alcohol (8 mL) and water (4 mL) was heated at reflux for 3 h. The mixture was quenched with dilute aqueous HCl, and the mixture was extracted with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give

a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane/ethyl acetate = 20:1) to afford **18a** (621 mg, 1.96 mmol, 98%).

Synthesis of Methyl 4'-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienylcarbonyl)biphenyl-4-carboxylate (18b)

A mixture of **4d** (479 mg, 1.50 mmol), *p*-methoxycarbonyphenylboronic acid (324 mg, 1.80 mmol), $Pd(OAc)_2$ (17.0 mg, 0.075 mmol), triphenylphosphine (59.0 mg, 0.23 mmol), and CsF (547 mg, 3.60 mmol) in dimethoxyethane (10 mL) was heated at reflux for 13 h. After the reaction was quenched with water, the mixture was extracted with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Silica gel column chromatography (Wakogel C-200, hexane/ethyl acetate = 20:1) provided **18b** (530 mg, 1.41 mmol, 94%).

Synthesis of 3-Biphenylyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (18c)

A mixture of **4e** (1.78 g, 6.48 mmol), phenylboronic acid (949 mg, 7.78 mmol), $Pd_2(dba)_3$ (297 mg, 0.32 mmol), tri(*t*-butyl)phosphine in hexane (1.0 M, 0.96 mL, 0.96 mmol), and KF (1.24 g, 21.4 mmol) in dioxane (13 mL) was heated at reflux for 72 h. The reaction was quenched with dilute aqueous HCl, and the mixture was extracted with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane/ethyl acetate = 80:1) to afford **18c** (1.16 g, 3.67 mmol, 57%).

Synthesis of 1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl (*E*)-4-stilbenyl ketone (20)

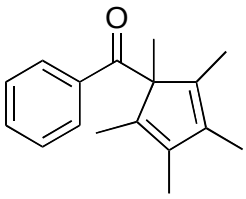
A solution of **4d** (319 mg, 1.00 mmol), styrene (0.23 mL, 2.00 mmol), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol), tri(*o*-tolyl)phosphine (30.4 mg, 0.10 mmol), and triethylamine (0.42 mL, 3.00 mmol) in DMF (1.2 mL) was heated at 120 ˚C for 26 h. After the reaction was quenched with saturated aqueous NH_4Cl, the mixture was extracted with hexane-ethyl acetate (5:1). The

combined organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Silica gel column chromatography (Wakogel C-200, hexane/ethyl acetate = 40:1) provided **20** (268 mg, 0.78 mmol, 78%).

Characterization Data

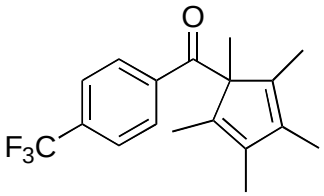
The spectral data of the products **8a**,[6] **8b**,[7] **8c**,[8] **8d**,[9] **8i**,[2a] **12**[10] and **16a**[11] can be found in the literature. Ketone **8h** is commercially available.

1,2,3,4,5-Pentamethyl–2,4–cyclopentadienyl phenyl ketone (4a)



IR (nujol) 1669 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (s, 3H), 1.68 (d, *J* = 1.0 Hz, 6H), 1.83 (d, *J* = 0.5 Hz, 6H), 7.20–7.25 (m, 2H), 7.36–7.41 (m, 1H), 7.50–7.54 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.60 (× 2), 11.41 (× 2), 19.19, 70.31, 127.32 (× 2), 127.88 (× 2), 131.86, 138.06 (× 2), 138.23, 140.00 (× 2), 202.37. Found: C, 84.85; H, 8.37%. Calcd for $C_{17}H_{20}O$: C, 84.96; H, 8.39%. m.p. 45.0–45.5 ˚C.

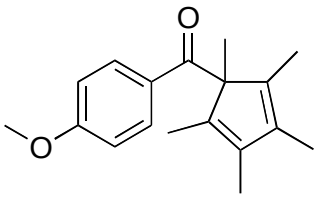
1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl 4-trifluoromethylphenyl ketone (4b)



IR (neat) 2921, 1674, 1325, 1169, 1130, 1068 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (s, 3H), 1.69 (s, 6H), 1.83 (s, 6H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 10.57 (× 2), 11.41 (× 2), 18.64, 70.40, 123.71 (q, *J* = 272.5 Hz), 124.91 (q, *J* = 3.9 Hz, × 2), 127.47 (× 2), 133.09 (q, *J* = 32.2 Hz), 138.99 (× 2), 139.36 (× 2), 141.10, 201.74. Found: C, 69.88; H,

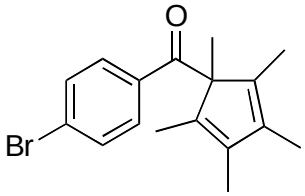
6.33%. Calcd for $C_{18}H_{19}F_3O$: C, 70.12; H, 6.21%.

4-Methoxyphenyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (4c)



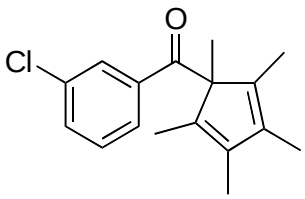
IR (nujol) 1656, 1600, 1572, 1248, 1176 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (s, 3H), 1.68 (d, *J* = 0.5 Hz, 6H), 1.85 (d, *J* = 0.5 Hz, 6H), 3.80 (s, 3H), 6.72 (d, *J* = 9.0 Hz, 2H), 7.60 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 10.55 (× 2), 11.37 (× 2), 19.82, 55.14, 69.98, 113.01 (× 2), 129.95 (× 2), 130.64, 137.19 (× 2), 140.94 (× 2), 162.65, 199.93. Found: C, 79.78; H, 8.14%. Calcd for $C_{18}H_{22}O_2$: C, 79.97; H, 8.20%. m.p. 135.0–136.0 ˚C.

4-Bromophenyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (4d)



IR (nujol) 1652, 1582 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (s, 3H), 1.67 (d, *J* = 1.0 Hz, 6H), 1.83 (s, 6H), 7.35–7.38 (m, 2H), 7.40–7.43 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.54 (× 2), 11.38 (× 2), 19.09, 70.17, 126.75, 129.00 (× 2), 131.10 (× 2), 136.65, 138.27 (× 2), 139.92 (× 2), 201.08. Found: C, 63.88; H, 5.98%. Calcd for $C_{17}H_{19}OBr$: C, 63.96; H, 6.00%. m.p. 58.0–59.0 ˚C.

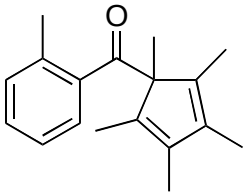
3-Chlorophenyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (4e)



IR (neat) 2972, 2916, 2855, 1674, 1668, 1569, 1443, 1230, 974 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23

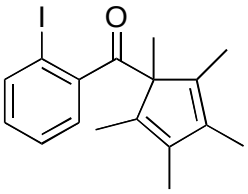
(s, 3H), 1.68 (s, 6H), 1.84 (s, 6H), 7.16 (t, *J* = 8.0 Hz, 1H), 7.33–7.42 (m, 2H), 7.51 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.61 (× 2), 11.42 (× 2), 18.78, 70.35, 125.36, 127.56, 129.23, 131.77, 133.86, 138.75 (× 2), 139.50, 139.67 (× 2), 201.09. Found: C, 74.04; H, 7.25%. Calcd for $C_{17}H_{19}ClO$: C, 74.31; H, 6.97%.

1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl *o*-tolyl ketone (4f)



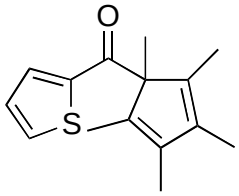
IR (nujol) 1681 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3H), 1.69 (d, *J* = 1.0 Hz, 6H), 1.77 (d, *J* = 0.5 Hz, 6H), 2.32 (s, 3H), 6.89–6.95 (m, 2H), 7.11–7.15 (m, 1H), 7.16–7.20 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 10.47 (× 2), 11.36 (× 2), 18.24, 20.47, 71.07, 124.69, 125.12, 129.66, 130.92, 135.44, 138.51 (× 2), 138.57 (× 2), 139.09, 206.12. Found: C, 84.71; H, 8.68%. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72%. m.p. 36.0–37.0 ˚C.

2-Iodophenyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (4g)



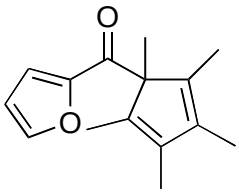
IR (nujol) 1684 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.76 (s, 12H), 6.86 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.97 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.08 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.83 (dd, *J* = 8.0, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.79 (× 2), 11.37 (× 2), 17.75, 70.77, 91.66, 125.43, 126.91, 130.85, 137.96 (× 2), 139.26 (× 2), 140.26, 143.68, 204.93. Found: C, 55.70; H, 5.18%. Calcd for $C_{17}H_{19}IO$: C, 55.75; H, 5.23%. m.p. 59.0–60.0 ˚C.

1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl 2-thienyl ketone (4h)



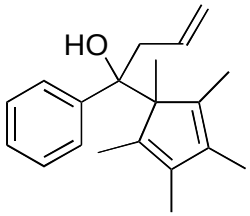
IR (nujol) 1638 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 3H), 1.71 (d, *J* = 0.5 Hz, 6H), 1.86 (d, *J* = 0.5 Hz, 6H), 6.92 (dd, *J* = 5.0, 4.0 Hz, 1H), 7.37 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.54 (dd, *J* = 4.0, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.53 (× 2), 11.46 (× 2), 17.63, 69.69, 127.07, 132.05, 132.13, 138.99 (× 2), 139.50 (× 2), 140.60, 193.31. Found: C, 72.96; H, 7.40%. Calcd for $C_{15}H_{18}OS$: C, 73.13; H, 7.36%. m.p. 85.5–86.5 ˚C.

2-Furyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (4i)



IR (nujol) 1653 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 3H), 1.70 (s, 6H), 1.85 (s, 6H), 6.28–6.32 (m, 1H), 6.73–6.77 (m, 1H), 7.44–7.49 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 10.48 (× 2), 11.42 (× 2), 17.51, 68.83, 111.51, 116.73, 137.91 (× 2), 139.68 (× 2), 145.90, 150.13, 189.08. Found: C, 77.95; H, 7.86%. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88%. m.p. 90.5–91.0 ˚C.

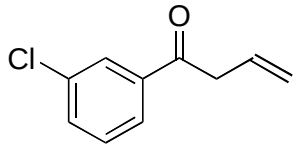
1-(1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl)-1-phenyl-3-buten-1-ol (7a)



IR (neat) 2917, 1445, 1327, 1249, 992, 924, 761, 709 cm^{-1}; ^{1}H NMR (C_6D_6) δ 1.31 (s, 3H), 1.45 (d, *J* = 1.5 Hz, 3H), 1.60 (d, *J* = 1.0 Hz, 3H), 1.86 (s, 3H), 1.96 (s, 3H), 2.03 (s, 1H), 2.47 (dd, *J* = 13.5, 10.0 Hz, 1H), 2.94 (ddt, *J* = 13.5, 5.0, 1.5 Hz, 1H), 4.80 (ddt, *J* = 10.0, 1.5, 0.5 Hz, 1H),

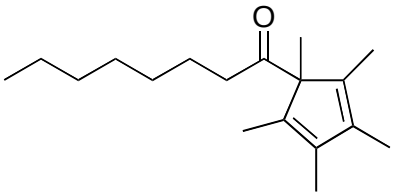
4.90–4.95 (m, 1H), 5.31 (dddd, *J* = 17.5, 10.0, 10.0, 5.0 Hz, 1H), 6.99–7.13 (m, 3H), 7.27–7.33 (m, 2H); ^{13}C NMR (C_6D_6) δ 10.86, 11.14, 13.46, 13.72, 15.86, 41.86, 63.72, 78.51, 120.04, 126.56, 126.62 (× 2), 126.65 (× 2), 134.60, 135.65, 137.74, 138.66, 141.65, 143.85. Found: C, 84.88%; H, 9.58. Calcd for $C_{20}H_{26}O$: C, 85.05; H, 9.28%.

Allyl 3-chlorophenyl ketone (8e)



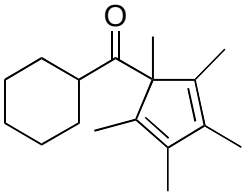
IR (nujol) 1679 cm^{-1}; ^{1}H NMR (C_6D_6) δ 3.08 (dt, *J* = 6.5, 1.5 Hz, 2H), 4.93 (ddt, *J* = 17.0, 3.0, 1.5 Hz, 1H), 5.03 (ddt, *J* = 10.5, 3.0, 1.5 Hz, 1H), 5.97 (ddt, *J* = 17.0, 10.5, 6.5 Hz, 1H), 6.73 (t, *J* = 8.0 Hz, 1H), 7.06–7.09 (m, 1H), 7.43–7.48 (m, 1H), 7.74–7.78 (m, 1H); ^{13}C NMR (C_6D_6) δ 43.07, 118.30, 126.33, 128.54, 129.93, 131.23, 132.69, 134.87, 138.48, 195.29. Found: C, 66.70%; H, 5.07. Calcd for $C_{10}H_9ClO$: C, 66.49; H, 5.02%. m.p. 32.0–33.0 ˚C.

Heptyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (14a)



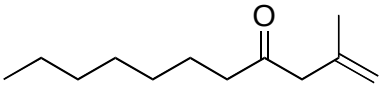
IR (neat) 2928, 1701 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.86 (t, *J* = 7.0 Hz, 3H), 1.09 (s, 3H), 1.67 (s, 6H), 1.84 (s, 6H), 1.13–1.42 (m 10H), 1.84 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 10.39 (× 2), 11.41 (× 2), 14.07, 14.70, 22.61, 24.03, 29.00, 29.20, 31.67, 34.63, 71.33, 136.98 (× 2), 139.38 (× 2), 210.42. Found: C, 82.14; H, 11.24%. Calcd for $C_{18}H_{30}O$: C, 82.38; H, 11.52%.

Cyclohexyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (14b)



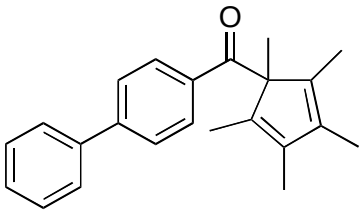
IR (neat) 2931, 2856, 1695, 1448, 989 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.99–1.67 (m, 10H), 1.08 (s, 3H), 1.69 (d, *J* = 1.0 Hz, 6H), 1.86 (d, *J* = 0.5 Hz, 6H), 2.05 (tt, *J* = 11.5, 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.94 (× 2), 11.44 (× 2), 14.62, 25.67 (× 2), 25.71, 30.01 (× 2), 43.22, 71.67, 136.55 (× 2), 139.94 (× 2), 213.51. Found: C, 82.58; H, 10.90%. Calcd for $C_{17}H_{26}O$: C, 82.87; H, 10.64%.

Heptyl 2-methyl-2-propenyl ketone (16b)



IR (neat) 2929, 1717, 1649, 1458, 1376, 894 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.89 (t, *J* = 7.0 Hz, 3H), 1.10–1.30 (m, 8H), 1.46–1.55 (m, 2H), 1.66 (s, 3H), 2.07 (t, *J* = 7.0 Hz, 2H), 2.77 (d, *J* = 1.0 Hz, 2H), 4.70–4.74 (m, 1H), 4.82–4.86 (m, 1H); ^{13}C NMR (C_6D_6) δ 14.27, 22.59, 22.98, 23.96, 29.45, 29.48, 32.04, 41.67, 52.09, 114.48, 140.01, 206.43. Found: C, 79.32; H, 12.37%. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16%.

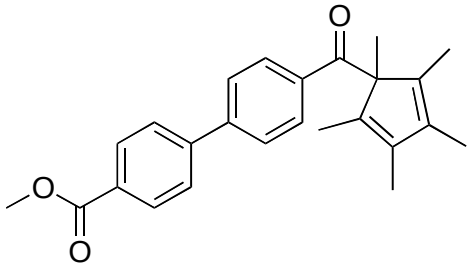
4-Biphenylyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (18a)



IR (nujol) 1653 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3H), 1.72 (s, 6H), 1.87 (s, 6H), 7.33–7.38 (m, 1H), 7.41–7.49 (m, 4H), 7.56–7.59 (m, 2H), 7.62–7.66 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.66 (× 2), 11.46 (× 2), 19.38, 70.30, 126.56 (× 2), 127.06 (× 2), 127.84, 128.06 (× 2), 128.78 (× 2), 136.78, 137.96 (× 2), 140.08, 140.26 (× 2), 144.50, 201.67. Found: C, 87.24; H, 7.68%. Calcd

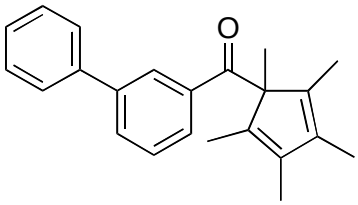
for $C_{23}H_{24}O$: C, 87.30; H, 7.64%. m.p. 90.0–91.0 ˚C.

Methyl 4'-(1,2,3,4,5-pentamethyl-2,4-cyclopentadienylcarbonyl)biphenyl-4-carboxylate (18b)



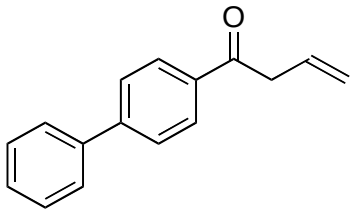
IR (nujol) 1722, 1663, 1604, 1277, 1108 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3H), 1.71 (s, 6H), 1.86 (s, 6H), 3.93 (s, 3H), 7.48–7.51 (m, 2H), 7.62–7.66 (m, 4H), 8.07–8.11(m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.66 (× 2), 11.47 (× 2), 19.26, 52.17, 70.35, 126.79 (× 2), 127.02 (× 2), 128.12 (× 2), 129.39, 130.10 (× 2), 137.57, 138.18 (× 2), 140.13 (× 2), 143.18, 144.50, 166.85, 201.66. Found: C, 79.89; H, 7.02%. Calcd for $C_{25}H_{26}O_3$: C, 80.18; H, 7.00%. m.p. 123.0–124.0 ˚C.

3-Biphenylyl 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl ketone (18c)



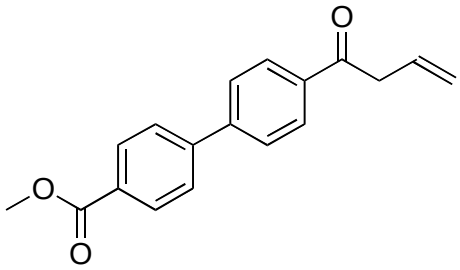
IR (neat) 2918, 1668, 1451, 1218, 971, 760, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3H), 1.73 (s, 6H), 1.88 (s, 6H), 7.31–7.38 (m, 2H), 7.42–7.46 (m, 2H), 7.48–7.53 (m, 2H), 7.56–7.60 (m, 1H), 7.64–7.67 (m, 1H), 7.86–7.89 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 10.67 (× 2), 11.47 (× 2), 19.28, 70.39, 126.20, 126.35, 126.77 (× 2), 127.45, 128.44, 128.75 (× 2), 130.37, 137.99 (× 2), 138.43, 140.36, 140.53 (× 3), 201.98. HRMS Found: 316.1826. Calcd for $C_{23}H_{24}O$: 316.1827.

Allyl 4-biphenylyl ketone (19a)



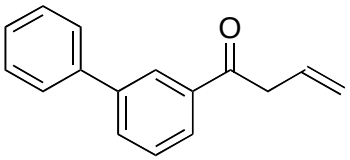
IR (nujol) 1684 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.80 (dt, *J* = 7.0, 1.5 Hz, 2H), 5.25 (ddt, *J* = 17.0, 3.0, 1.5 Hz, 1H), 5.26 (ddt, *J* = 10.5, 3.0, 1.5 Hz, 1H), 6.12 (ddt, *J* = 17.0, 10.5, 7.0 Hz, 1H), 7.39–7.43 (m, 1H), 7.45–7.50 (m, 2H), 7.62–7.65 (m, 2H), 7.68–7.71 (m, 2H), 8.03–8.07 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 43.52, 118.76, 127.27 (× 4), 128.25, 128.89 (× 2), 128.95 (× 2), 131.10, 135.25, 139.84, 145.86, 197.62. Found: C, 86.15; H, 6.55%. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.35%. m.p. 69.5–70.0 ˚C.

Methyl 4'-(3-butenoyl)biphenyl-4-carboxylate (19b)



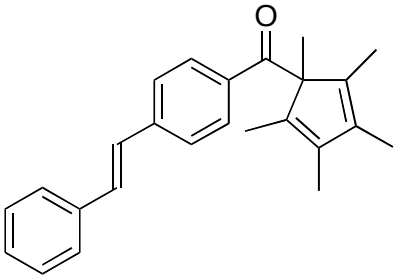
IR (nujol) 1723, 1677, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.80 (dt, *J* = 6.5, 1.5 Hz, 2H), 3.95 (s, 3H), 5.24 (ddt, *J* = 17.0, 2.5, 1.0 Hz, 1H), 5.26 (ddt, *J* = 10.5, 2.5, 1.0 Hz, 1H), 6.11 (ddt, *J* = 17.0, 10.5, 6.5 Hz, 1H), 7.66–7.74 (m, 4H), 8.03–8.08 (m, 2H), 8.11–8.15 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 43.52, 52.21, 118.86, 127.20 (× 2), 127.46 (× 2), 128.94 (× 2), 129.74, 130.20 (× 2), 130.90, 135.86, 144.11, 144.49, 166.73, 197.50. Found: C, 76.87; H, 5.74%. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75%. m.p. 139.0–140.0 ˚C.

Allyl 3-biphenylyl ketone (19c)



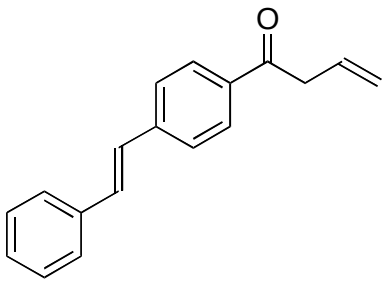
IR (neat) 3032, 1687, 1598, 1478, 1452, 1418, 1296, 1188, 921 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.82 (dt, *J* = 7.0, 1.5 Hz, 2H), 5.25 (ddt, *J* = 17.0, 3.5, 1.5 Hz, 1H), 5.27 (ddt, *J* = 10.5, 3.5, 1.5 Hz, 1H), 6.13 (ddt, *J* = 17.0, 10.5, 7.0 Hz, 1H), 7.37–7.42 (m, 1H), 7.46–7.50 (m, 2H), 7.52–7.57 (m, 1H), 7.60–7.64 (m, 2H), 7.77–7.82 (m, 1H), 7.94–7.96 (m, 1H), 8.19–8.21 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 43.58, 118.80, 126.95, 127.08, 127.16 (× 2), 127.80, 128.91 (× 2), 129.06, 131.00, 131.78, 137.04, 140.12, 141.75, 197.95. Found: C, 86.57; H, 6.54%. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.35%.

1,2,3,4,5-Pentamethyl-2,4-cyclopentadienyl (*E*)-4-stilbenyl ketone (20)



IR (nujol) 1661, 1604 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 3H), 1.70 (d, *J* = 1.0 Hz, 6H), 1.86 (d, *J* = 0.5 Hz, 6H), 7.04 (d, *J* = 16.5 Hz, 1H), 7.14 (d, *J* = 16.5 Hz, 1H), 7.25–7.30 (m, 1H), 7.34–7.39 (m, 4H), 7.48–7.52 (m, 2H), 7.54–7.58 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.64 (× 2), 11.45 (× 2), 19.42, 70.29, 125.97 (× 2), 126.68 (× 2), 127.75, 128.05, 128.07 (× 2), 128.73 (× 2), 130.54, 136.91, 136.98, 137.90 (× 2), 140.35 (× 2), 140.84, 201.31. Found: C, 87.41; H, 7.76%. Calcd for $C_{25}H_{26}O$: C, 87.68; H, 7.65%. m.p. 106.0–107.0 ˚C.

Allyl (*E*)-4-stilbenyl ketone (21)



IR (nujol) 1685, 969, 818, 722 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.77 (d, *J* = 6.5 Hz, 2H), 5.20–5.28 (m, 2H), 6.10 (ddt, *J* = 17.0, 10.5, 6.5 Hz, 1H), 7.14 (d, *J* = 16.5 Hz, 1H), 7.24 (d, *J* = 16.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 7.97 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 43.40, 118.68, 126.50 (× 2), 126.79 (× 2), 127.35, 128.30, 128.76 (× 2), 128.81 (× 2), 131.12, 131.48, 135.27, 136.62, 142.03, 197.30. Found: C, 86.93; H, 6.62%. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49%. m.p. 105.0–106.0 ˚C.

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(3) The reaction of **4a** with 1.5 equiv of an allylaluminum reagent, which was prepared from allyltributyltin, butyllithium, and dimethylaluminum chloride, at –20 ˚C for 1 h also afforded the 3-butenyl alcohol **7a** in 84% yield.

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Chapter 4

Synthesis of $Cp^*CH_2PPh_2$ and its Use as a Ligand for Nickel-Catalyzed Cross-Coupling Reaction of Alkyl Halides with Aryl Grignard Reagents

A new ligand, $Cp^*CH_2PPh_2$ (Cp^* = 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl), was prepared, and was used as a ligand for nickel-catalyzed cross-coupling reaction of alkyl halides with aryl Grignard reagents, which nickel-phosphine complexes had never made possible.

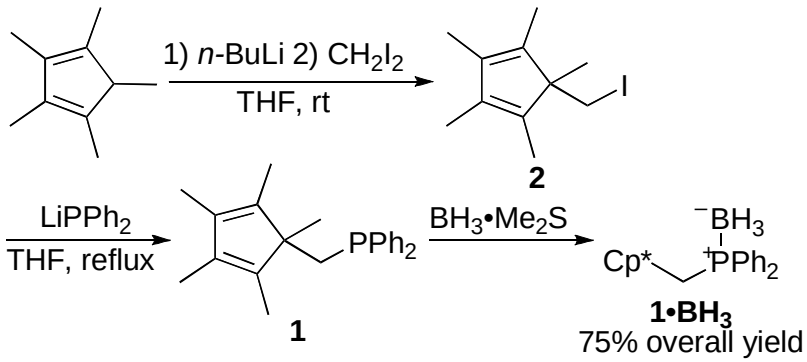
Introduction

Phosphine ligands play important roles in organic synthesis as clearly demonstrated in transition metal catalysis. Among them, monophosphine ligands having an additional intramolecular coordinating site are an important class.[1] Recently, monophosphine ligands having a coordinating alkene moiety was developed and applied to highly enantioselective transformations.[2] Here the author introduces $Cp^*CH_2PPh_2$ (**1**, Cp* = 1,2,3,4,5-pentamethyl-2,4-cyclopentadienyl), a monophosphine ligand with a pendant 1,3-diene moiety. He envisioned that the 1,3-diene part as well as the phosphorous atom would coordinate to transition metal and that **1** would thus serve as a new six-electron donating ligand.

Results and Discussion

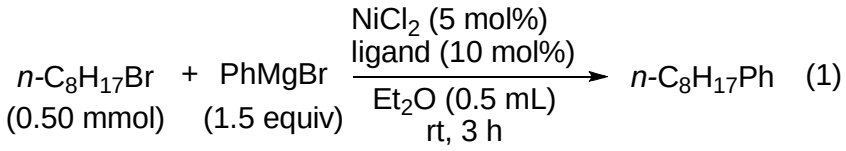
The synthesis of **1** is outlined in Scheme 1. The reaction of Cp*Li with diiodomethane provided iodide **2**. Treatment of **2** with lithium diphenylphosphide in refluxing THF afforded **1** in high yield. Since **1** is sensitive to oxygen, the author converted the ligand to a phosphine-borane complex and handled it. The phosphine **1** was regenerated in situ by removing borane with 1,8-diazabicyclo[2.2.2]octane (DABCO) prior to use as a ligand.

Scheme 1.



Cross-coupling reactions of alkyl halides are rather difficult reactions, compared to those of aryl or alkenyl halides, since intermediary alkylmetal complexes are prone to undergo

β-hydride elimination.[3,4] The author expected that the diene moiety of **1** could advantageously occupy vacant coordination sites necessary for the β-hydride elimination. He thus chose nickel-catalyzed cross-coupling reaction of 1-bromooctane with phenylmagnesium bromide as a model reaction (eq. 1, Table 1). Although several nickel complexes catalyze such a difficult coupling reaction,[3b,3c,4] there are no reports on the cross-coupling reaction catalyzed by nickel-phosphine complexes.[5]



The nickel-catalyzed reaction using **1** was indeed successful, yielding octylbenzene quantitatively (entry 1).[6,7] A mixture of **1** (27 μmol, 54% recovery) and the oxide of **1** (22 μmol, 43% recovery) were obtained from the reaction mixture. The recovery of these compounds suggests that a bis(π-allyl)nickel complex which is a suitable catalyst for similar coupling reactions[3b] is not generated from **1** in the reaction mixture.

Other conventional phosphines such as triphenylphosphine, tricyclohexylphosphine, and tri(*t*-butyl)phosphine did not assist the coupling reaction efficiently (entries 2–4). Use of neopentyldiphenylphosphine that is as bulky as **1** failed to afford octylbenzene (entry 5). It is worth noting that a homologue of **1**, Cp*$CH_2CH_2PPh_2$ (**3**), was far less effective (entry 6). Hexamethylcyclopentadiene (**4**) is not a suitable ligand by itself (entry 7). Interestingly, combined use of **4** and triphenylphosphine resulted in formation of octylbenzene in moderate yield (entry 8). Without any ligands, octylbenzene was obtained in only 5% yield (entry 9).

Table 1. Effect of Ligands on Nickel-Catalyzed Cross-Coupling Reaction of 1-Bromooctane with Phenylmagnesium Bromide[a]

entry	ligand	NMR yield /%[d]
1	**1**[b]	88
2	PPh_3	24
3	P(*c*-C_6H_{11})$_3$	12
4	P(*t*-Bu)$_3$	9
5	*t*-BuCH_2PPh_2[b]	7
6	Cp*$CH_2CH_2PPh_2$[b]	11
7	Cp*Me	3
8	Cp*Me + PPh_3[c]	31
9	none	4

[a] Reaction conditions are shown in eq. 1. [b] Generated *in situ* by treatment of the relevant phoshphine-borane with 1,8-diazabicyclo[2.2.2]octane (DABCO). [c] 10 mol% of both **4** and triphenylphosphine. [d] The yields were determined as follows. After extractive workup and evaporation, bromoform was added to a crude oil. Comparison of the ^{1}H signals of bromoform and octylbenzene revealed the NMR yield.

Diethyl ether is the best solvent. The reactions in toluene, THF, dioxane, and hexane provided octylbenzene in 73, 67, 54, and 53% yields, respectively, under the $NiCl_2$(**1**) catalysis.

Other alkyl halides also underwent the nickel-catalyzed phenylation with the aid of **1** (eq. 2, Table 2). The reactions of primary alkyl bromides provided the corresponding phenylated products in high yields (entries 1, 2, 4–9). Typical protective groups such as THP and 1,3-dioxolane survived under the reaction conditions (entries 6, 7), while carbonyl groups

were not tolerant. 8-Bromo-1-octene was phenylated, leaving the terminal olefinic group untouched (entry 9). Primary alkyl iodide was as reactive as bromide (entry 3). In contrast, alkyl chloride was inactive. Unfortunately, an attempted cross-coupling reaction of secondary alkyl bromide resulted in the formation of cyclohexylbenzene in an unsatisfactory yield (entry 10).

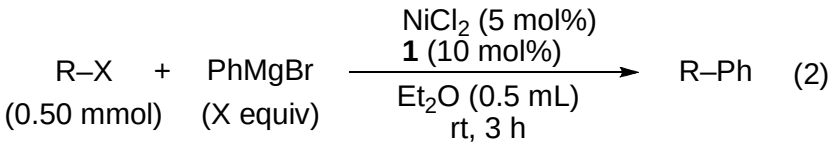


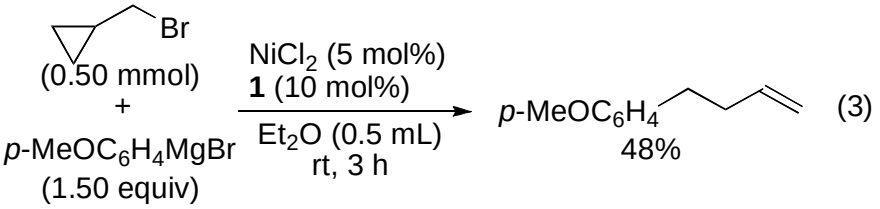
Table 2. Reactions of Various Alkyl Halides with Phenylmagnesium Bromide[a]

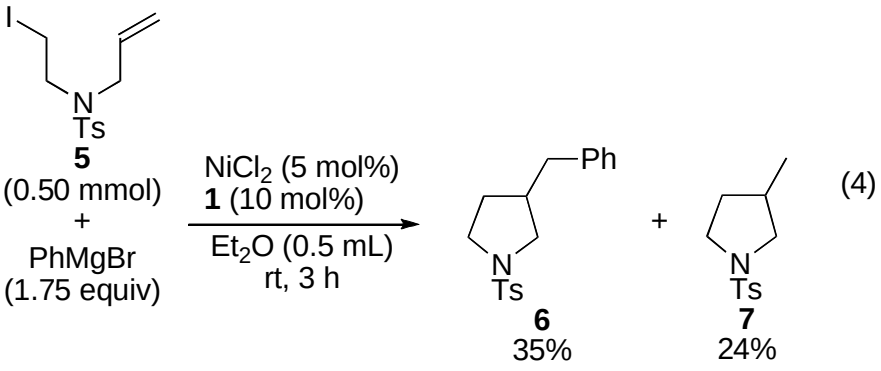
entry	substrate	X equiv	isolated yield /%
1	*n*-$C_8H_{17}Br$	1.50	83
2	*n*-$C_8H_{17}Br$	1.50	84[b]
3	*n*-$C_{12}H_{25}I$	1.75	60
4	$PhCH_2CH_2Br$	1.75	60
5	$PhCH_2CH_2CH_2Br$	1.75	70
6	$THPO(CH_2)_5Br$[c]	1.75	76
7	$(OCH_2CH_2O)CH(CH_2)_4Br$	2.50	76
8	$Br(CH_2)_6Br$	3.00	68[d]
9	$CH_2=CH(CH_2)_6Br$	2.00	62
10	*c*-$C_6H_{11}Br$	1.50	36

[a] Reaction conditions are shown in eq. 2. Ligand **1** was generated *in situ* by treatment of **1•BH$_3$** with DABCO. [b] *p*-$MeOC_6H_4MgBr$ was used instead of PhMgBr. [c] THP = Tetrahydropyranyl. [d] Product is $Ph(CH_2)_6Ph$.

The following two experiments suggest that the cross-coupling reaction would involve

a radical process. Treatment of cyclopropylmethyl bromide with *p*-methoxyphenylmagnesium bromide furnished *p*-(3-butenyl)anisole (eq. 3). No cyclopropane skeletons were observed in the crude oil. In addition, the reaction of 6-halo-1-hexene derivative **5** afforded benzyl-substituted pyrrolidine **6**, in addition to unphenylated pyrrolidine **7** (eq. 4). Ring-opening of a cyclopropylmethyl radical and ring-closure of a 5-hexenyl radical are well-known isomerization reactions,[8] suggesting the intermediacy of carbon-centered radicals. Oxidative addition via a single electron transfer process is most probable.[3f]





Experimental Section

Synthesis of 1•BH_3

A solution of butyllithium in hexane (1.60 M, 8.75 mL, 14 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (2.5 mL, 15 mmol) in THF (50 mL) at –20 ˚C. The mixture was stirred for 30 min at the same temperature. Diiodomethane (0.81 mL, 10 mmol) was added to the reaction mixture, and the mixture was stirred for 12 h at room temperature. The reaction was quenched with water, and the mixture was extracted with hexane. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was filtered through a short pad of silica gel (Wakogel C-200, hexane) to afford 5-iodomethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene, which was used for the next step without further purification. A solution of butyllithium in hexane (1.60 M, 5.29 mL, 8.46 mmol) was added to a solution of diphenylphosphine (1.33 mL, 7.69 mmol) in THF (38 mL) at 0 ˚C. The mixture was stirred for 10 min at the same temperature. 5-Iodomethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene in THF (10 mL) was added to the reaction mixture, and the mixture was stirred for 3 h at 70 ˚C. Borane-dimethyl sulfide complex (0.88 mL, 9.23 mmol) was added to the mixture at 0 ˚C, and the resulting mixture was stirred for 30 min at 0 ˚C. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane - ethyl acetate=20:1) to afford **1•BH_3** (2.02 g, 5.80 mmol, 75%).

Preparation of Phosphine-Borane Complex, *t*-$BuCH_2PPh_2$•BH_3 (Table 1, entry 5)

A solution of butyllithium in hexane (1.58 M, 2.78 mL, 4.4 mmol) was added to a solution of diphenylphosphine (0.69 mL, 4.0 mmol) in THF (20 mL) at 0 ˚C. The mixture was stirred for 10 min at the same temperature. Neopentyl iodide (0.64 mL, 4.8 mmol) was added to the reaction mixture, and the mixture was stirred for 3 h at 70 ˚C. Borane-dimethyl sulfide

complex (0.46 mL, 4.8 mmol) was added to the mixture at 0 ˚C, and the resulting mixture was stirred for 30 min at 0 ˚C. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane - ethyl acetate=20:1) to afford *t*-$BuCH_2PPh_2$•BH_3 (940 mg, 3.48 mmol, 87%).

Preparation of Phosphine-Borane Complex, Cp*$CH_2CH_2PPh_2$•BH_3 (Table 1, entry 6)

A solution of butyllithium in hexane (1.58 M, 6.96 mL, 11 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (1.72 mL, 11 mmol) in THF (50 mL) at –20 ˚C. The mixture was stirred for 30 min at the same temperature. 1, 2-Dibromoethane (0.86 mL, 10 mmol) was added to the reaction mixture, and the mixture was stirred for 12 h at 70 ˚C to afford 5-(2-bromoethyl)-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene. The solution was used for the next step without quenching. A solution of butyllithium in hexane (1.58 M, 7.59 mL, 12 mmol) was added to a solution of diphenylphosphine (2.07 mL, 12 mmol) in THF (50 mL) at 0 ˚C. The mixture was stirred for 10 min at the same temperature. The solution of 5-(2-bromoethyl)-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene was added to the reaction mixture, and the mixture was stirred for 8 h at 70 ˚C. Borane-dimethyl sulfide complex (1.23 mL, 13 mmol) was added to the mixture at 0 ˚C, and the resulting mixture was stirred for 30 min at 0 ˚C. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane - ethyl acetate=30:1) to afford Cp*$CH_2CH_2PPh_2$•BH_3 (2.33 g, 6.43 mmol, 64%).

General Procedure for Nickel-Catalyzed Coupling Reaction

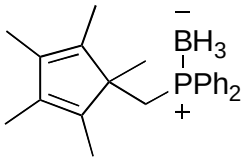
$NiCl_2$ (3.2 mg, 0.025 mmol), phosphine-borane complex **1•BH_3** (17.4 mg, 0.050 mmol), and 1,8-diazabicyclo[2.2.2]octane (8.4 mg, 0.075 mmol) in toluene (0.2 mL) were stirred for 30

min at 60 ˚C. Diethyl ether (0.5 mL) and 1-bromooctane (0.086 mL, 0.50 mmol) were added to the resulting mixture. Phenylmagnesium bromide in THF (1.99 M, 0.38 mL, 0.75 mmol) was added to the reaction mixture. The mixture was stirred for 3 h at room temperature. The reaction was quenched with saturated ammonium chloride solution, and the mixture was extracted with hexane. The combined organic layer was dried over Na_2SO_4 and concentrated. Silica gel column purification (Wakogel C-200, hexane) of the crude product provided octylbenzene (78.9 mg, 0.41 mmol, 83%). Octylbenzene was visualized by UV on TLC.

Characterization Data

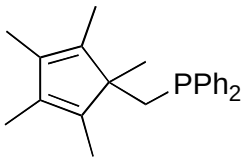
The products (entry 1–5, 8, and 10) in Table 2 and in eq. 3 are commercially available, and showed reasonable ^{1}H NMR spectra. Compounds in eq. 4 are found in the literature.[10]

1•BH_3



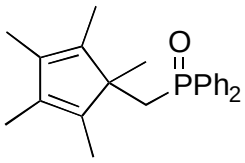
IR (nujol) 694, 736, 866, 1058, 1436, 2385 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.40–1.20 (br, 3H), 0.98 (d, *J* = 2.5 Hz, 3H), 1.39 (s, 6H), 1.59 (s, 6H), 2.53 (d, *J* = 11.0 Hz, 2H), 7.33–7.56 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 10.09 (× 2), 11.02 (× 2), 24.87 (d, *J* = 13.8 Hz), 31.31 (d, *J* = 32.9 Hz), 53.51, 128.00 (d, *J* = 9.5 Hz, × 4), 130.47 (d, *J* = 2.4 Hz, × 2), 131.12 (d, *J* = 54.9 Hz, × 2), 132.56 (d, *J* = 9.1 Hz, × 4), 135.75 (× 2), 138.21 (× 2); ^{31}P NMR ($CDCl_3$) δ 9.08 (m). Found: C, 79.11; H, 8.62%. Calcd for $C_{23}H_{30}BP$: C, 79.32; H, 8.68%. m.p. 85.0–85.5 ˚C.

Phosphine 1



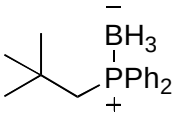
^{1}H NMR ($CDCl_3$) δ 0.96 (d, *J* = 1.8 Hz, 3H), 1.38 (d, *J* = 0.9 Hz, 6H), 1.71 (d, *J* = 0.9 Hz, 6H), 2.26 (d, *J* = 3.0 Hz, 2H), 7.20–7.35 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 9.6 (d, *J* = 2.9 Hz, × 2), 10.91 (× 2), 23.52 (d, *J* = 7.6 Hz), 35.32 (d, *J* = 13.9 Hz), 54.60 (d, *J* = 15.3 Hz), 127.80 (d, *J* = 6.3 Hz, × 4), 127.94 (× 2), 128.62 (d, *J* = 101.6 Hz, × 2), 133.26 (d, *J* = 19.5 Hz, × 4), 134.57 (× 2), 140.02 (d, *J* = 2.9 Hz, × 2); ^{31}P NMR (C_6D_6) δ –23.58.

The oxide of 1



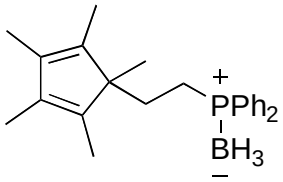
^{1}H NMR ($CDCl_3$) δ 0.97 (d, *J* = 2.7 Hz, 3H), 1.49 (d, *J* = 0.3 Hz, 6H), 1.59 (d, *J* = 0.6 Hz, 6H), 2.54 (d, *J* = 11.1 Hz, 2H), 7.34–7.64 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 10.02 (× 2), 10.85 (× 2), 24.96 (d, *J* = 16.8 Hz), 34.46 (d, *J* = 72.0 Hz), 53.00 (d, *J* = 3.3 Hz), 127.95 (d, *J* = 11.4 Hz, × 4), 130.79 (d, *J* = 9.0 Hz, × 4), 131.28 (d, *J* = 2.4 Hz, × 2), 133.33 (d, *J* = 98.3 Hz, × 2), 135.01 (× 2), 138.79 (× 2); ^{31}P NMR (C_6D_6) δ 20.16.

***t*-BuCH$_2$PPh$_2$•BH$_3$**



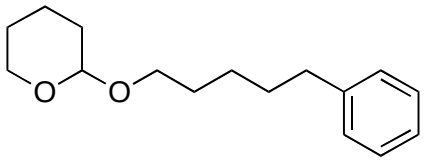
IR (nujol) 823, 1000, 1025, 1062, 1108, 1136, 1239, 1365, 1436, 2368 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80–1.55 (br, 3H), 1.02 (s, 9H), 2.37 (d, *J* = 12.0 Hz, 2H), 7.38–7.78 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 31.57 (d, *J* = 5.8 Hz, × 3), 32.40, 40.04 (d, *J* = 30.6 Hz), 128.63 (d, *J* = 10.0 Hz, × 4), 130.82 (d, *J* = 2.4 Hz, × 2), 131.31 (d, *J* = 54.9 Hz, × 2), 132.10 (d, *J* = 9.1 Hz, × 4); ^{31}P NMR ($CDCl_3$) δ 9.04 (m). Found: C, 75.19; H, 8.81%. Calcd for $C_{17}H_{24}BP$: C, 75.58; H, 8.95%. m.p. 141.5–143.0 ˚C.

Cp*$CH_2CH_2PPh_2$•BH_3



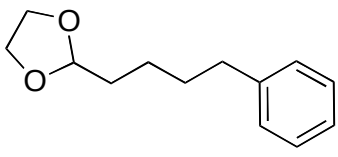
IR (nujol) 696, 737, 955, 999, 1066, 1106, 1436, 2364 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.50–1.35 (br, 3H), 0.83 (s, 3H), 1.40–1.60 (m, 10H), 1.78 (s, 6H), 7.37–7.63 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 9.53 (× 2), 11.06 (× 2), 19.88 (d, *J* = 37.8 Hz), 21.60, 27.56, 55.90 (d, *J* = 13.4 Hz), 128.69 (d, *J* = 9.5 Hz, × 4), 129.75 (d, *J* = 54.9 Hz, × 2), 131.01 (d, *J* = 2.4 Hz, × 2), 132.14 (d, *J* = 9.1 Hz, × 4), 134.83 (× 2), 138,94 (× 2); ^{31}P NMR ($CDCl_3$) δ 14.51 (m). Found: C, 79.44; H, 9.01%. Calcd for $C_{24}H_{32}BP$: C, 79.56; H, 8.90%. m.p. 103.0–103.5 ˚C.

5-Phenylpentyl 2-tetrahydropyranyl ether (Table 2, entry 6)



IR (neat) 699, 747, 870, 1023, 1078, 1121, 1201, 1353, 1453, 1496, 2858, 2937 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38–1.92 (m, 12H), 2.62 (t, *J* = 7.8 Hz, 2H), 3.34–3.58 (m, 2H), 3.68–3.94 (m, 2H), 4.57 (t, *J* = 4.5 Hz, 1H), 7.18–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 19.67, 25.47, 25.89, 29.58, 30.74, 31.35, 35.88, 62.34, 67.51, 98.84, 125.59, 128.22 (× 2), 128.39 (× 2), 142.68. Found: C, 77.17; H, 9.80%. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74%.

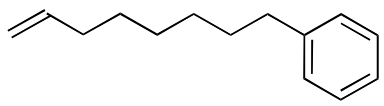
4-Phenyl-1-(2, 5-dioxacyclopentyl)butane (Table 2, entry 7)



IR (neat) 699, 749, 858, 945, 1030, 1134, 1360, 1410, 1454, 1496, 1604, 2860 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44–1.74 (m, 6H), 2.63 (t, *J* = 7.7 Hz, 2H), 3.80–4.00 (m, 4H), 4.85 (t, *J* = 4.8 Hz,

1H), 7.14–7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 23.81, 31.43, 33.76, 35.88, 64.83 (× 2), 104.54, 125.63, 128.25 (× 2), 128.38 (× 2), 142.50. Found: C, 75.90; H, 8.90%. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80%.

7-Octenylbenzene (Table 2, entry 9)



IR (neat) 698, 725, 746, 909, 994, 1030, 1453, 1496, 1605, 1641, 2855, 2929 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28–1.69 (m, 8H), 2.00–2.10 (m, 2H), 2.61 (t, *J* = 7.8 Hz, 2H), 4.90–5.04 (m, 2H), 5.81 (ddt, *J* = 6.6, 10.2, 17.1 Hz, 1H), 7.14–7.32 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 28.82, 28.96, 29.13, 31.44, 33.76, 35.94, 114.16, 125.54, 128.20 (× 2), 128.38 (× 2), 139.15. 142.86. Found: C, 89.14; H, 10.77%. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71%.

References and Notes

(1) Selected examples: Phosphine-phosphite ligand for asymmetric hydrophosphination, K. Nozaki, N. Sakai, T. Nanno, T. Higashijima, S. Mano, T. Horiuchi, H. Takaya, *J. Am. Chem. Soc.* **1997**, *119*, 4413. Aminophosphine ligand, T. Hayashi, K. Yamamoto, M. Kumada, *Tetrahedron Lett.* **1974**, *15*, 4005. Phosphinooxazole for hydrogenation, S. Bell, B. Wüstenberg, S. Kaiser, F. Menges, T. Netscher, A. Pfaltz, *Science* **2006**, *311*, 642.

(2) (a) R. Shintani, W.-L. Duan, T. Nagano, A. Okada, T. Hayashi, *Angew. Chem. Int. Ed.* **2005**, *44*, 4611. (b) R. Shintani, W.-L. Duan, K. Okamoto, T. Hayashi, *Tetrahedron Asymm.* **2005**, *16*, 3400.

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(4) The reactions in references 3b and 3c use 1,3-butadiene and pyridine derivatives, respectively, as a ligand. Nickel-salen complexes catalyzed phenylation of alkyl bromide: P. Styring, C. Grindon, C. M. Fisher, *Catal. Lett.* **2001**, *77*, 219.

(5) ^{31}P NMR analysis of a mixture of Ni(cod)$_2$ and **1** in C_6D_6 showed one clean signal at δ = 38.38ppm. A ^{31}P signal of **1** alone appeared at δ = –23.58ppm. The author is tempted to conjecture the formation of a nickel-phosphine complex. However, he has no clear evidence for the interaction between the diene moiety and the nickel. There remains a possibility that nickel-nanoparticles were formed. See ref 3g. .

(6) The reaction using BH_3-free ligand **1** also yielded octylbenzene quantitatively. DABCO has no influence on the reaction. We preferred using **1•BH$_3$** because of easy handling.

(7) The reaction of 1-bromooctane proceeded under the catalysis of $NiCl_2$ (5 mol%) and **1** (5 mol%) to afford octylbenzene quantitatively. However, in some cases in Table 2 and eq. 3

and 4, $NiCl_2$ (5 mol%) and double amount of **1** (10 mol%) were required to guarantee high yields.

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Chapter 5

Cp*Li as a Base: Application to Palladium-Catalyzed Cross-Coupling Reaction of Aryl-X or Alkenyl-X (X = I, Br, OTf, ONf) with Terminal Acetylenes

The reaction of aryl-X or alkenyl-X (X = I, Br, OTf, ONf) with terminal acetylenes in the presence of a catalytic amount of $Pd(OAc)_2$ provided the alkynylated products in good yield by using Cp*Li (Cp* = 1,2,3,4,5-pentamethylcyclopentadienyl) as a base.

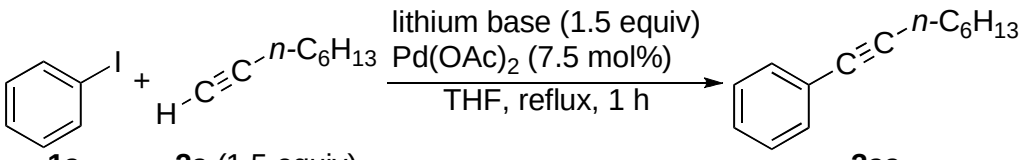
Introduction

Pentamethylcyclopentadienide ($Me_5C_5^-$, Cp^{*-}) has been used as a ligand of transition metal complexes for forty years.[1] Although Cp^{*-} has unique properties, such as six-electron donation and steric bulkiness by the five methyl groups on the five-membered ring, it has not been used for other purposes. Then the author has been exploring applications of Cp^{*-} as a reagent in organic synthesis.[2] Now, he has been interested in Cp^{*-} as a base. He expected that its strong basicity and steric bulkiness would exhibit interesting reactivities. Indeed, he has found that the reaction of aryl-X or alkenyl-X (X = I, Br, OTf, ONf) with terminal acetylenes in the presence of a catalytic amount of palladium provided the alkynylated products in good yields by using Cp*Li as a base.

Results and Discussion

Treatment of a suspension of Cp*Li in THF with iodobenzene (**1a**), 1-octyne (**2a**), and a catalytic amount of $Pd(OAc)_2$ at reflux for 1 h gave 1-octynylbenzene (**3aa**) in 82% yield (Table 1, entry 7). Other lithium bases, such as butyllithium, lithium diisopropylamide (LDA), lithium hexamethyldisilazide (LHMDS), and lithium cyclopentadienide (CpLi) did not assist the coupling reaction efficiently (entries 1–4). However, the use of lithium indenide resulted in formation of **3aa** in 24% yield (entry 5). Interestingly, the reaction with lithium tetramethylcyclopentadienide, which lacks one methyl group compared with Cp*Li, gave **3aa** in lower yield than that with Cp*Li yet in higher yield than that with CpLi (entry 6).

Table 1. Effect of Lithium Bases on Palladium-Catalyzed Cross-Coupling Reaction of Iodobenzene (**1a**) with 1-Octyne (**2a**)

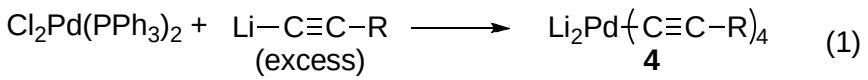


1a **2a** (1.5 equiv) **3aa**

entry	lithium base	NMR yield /%
1	butyllithium	3
2	lithium diisopropylamide (LDA)	3
3	lithium hexamethyldisilazide (LHMDS)	3
4	lithium cyclopentadienide (CpLi)	3
5	lithium indenide[a]	24
6	lithium tetramethylcyclopentadienide	55
7	Cp*Li	82[b]

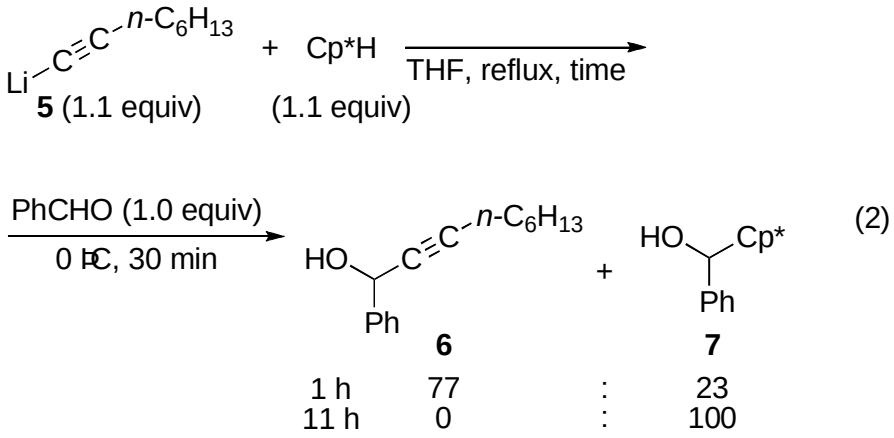
[a] Derived from indene and butyllithium. [b] Isolated yield

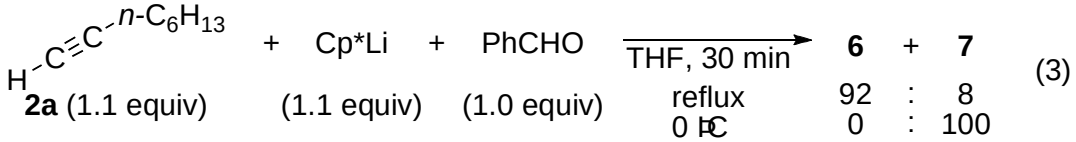
Although many kinds of alkynylmetals have been used for palladium-catalyzed cross-coupling reaction of aryl-X or alkenyl-X, there are no reports on the cross-coupling reaction with lithium acetylides.[3] The coupling reaction with lithium acetylides is difficult because the reaction of a palladium catalyst with an excess amount of lithium acetylides provides lithium palladate **4**, which does not exhibit any catalytic activity (eq. 1).[4] The author thought that gradual formation of lithium acetylides by means of Cp*Li would avoid the formation of **4**.

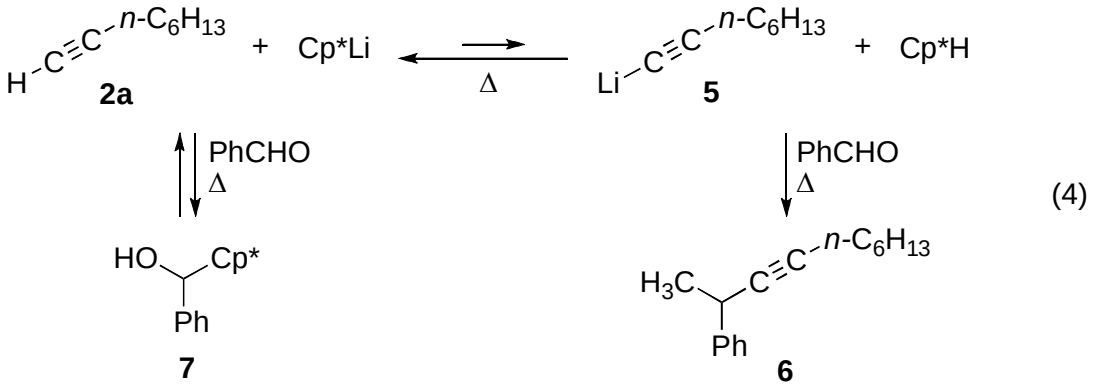


To confirm the gradual generation of lithium acetylides, the author carried out the following experiments. Treatment of lithium acetylide **5** with Cp*H for 1 h at reflux followed

by an addition of benzaldehyde at 0 ˚C gave a mixture of octynylated alcohol **6** and pentamethylcyclopentadienylated alcohol **7** (eq. 2). On the other hand, **7** was obtained selectively by using the reaction mixture of **5** and Cp*H which was heated for 11 h at reflux. These facts indicate that the pKa value of Cp*H is smaller than that of **2a** and that a high energy barrier exists between **2a** + Cp*Li and **5** + Cp*H. A similar reaction with cyclopentadiene (CpH), instead of Cp*H, only for 1 h followed by an addition of benzaldehyde did not give **6** but gave Cp adduct-derived compounds such as 6-phenylfulvene. This result means that the energy barrier between **2a** + CpLi and **5** + CpH is lower than that between **2a** + Cp*Li and **5** + Cp*H. Not only the pKa values of lithium bases but also the high energy barrier is important to promote the cross-coupling reaction. The reaction of a mixture of **2a** and Cp*Li with benzaldehyde at reflux or at 0 ˚C provided **6** or **7**, respectively (eq. 3). The results mean that **5** is generated only at reflux. The reason why **7** is not provided at reflux conditions is that nucleophilic addition reaction of Cp*Li to benzaldehyde is thermally reversible and that of **5** to benzaldehyde is irreversible (eq. 4). He is sure that the equilibrium between **2a** + Cp*Li and **5** + Cp*H is mostly biased toward **2a** + Cp*Li and that a modest amount of **5** + Cp*H would be generated at reflux.



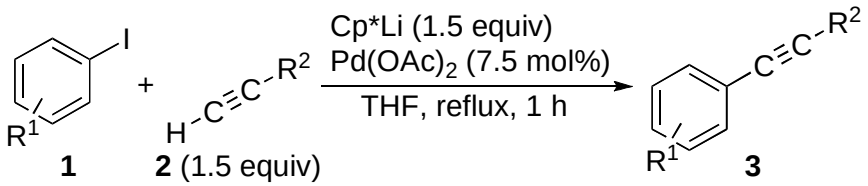




(4)

Table 2 summarizes the results obtained by the Cp*Li-mediated reaction of aryl iodides **1** with terminal acetylenes **2**. Aromatic iodide **1** bearing an electron-donating group (Table 2, entry 7) or an electron-withdrawing group (entry 8) afforded **3** in high yields. Surprisingly, ester (entry 10) or cyano moiety (entry 11) on the aromatic ring did not undergo nucleophilic addition reaction of Cp*Li or lithium acetylides during thermal conditions. Reaction of *meta*- or *ortho*-substituted **1** also proceeded smoothly (entries 12, 13). 1-Naphthyl iodide could be used in this reaction (entry 14). The reaction with phenylacetylene (**2c**) or trimethylsilylacetylene (**2e**) afforded **3** in good yields by using 15 mol% of triphenylphosphine (entries 3, 5).

Table 2. Reactions of Various Aryl Iodides **1** with Terminal Acetylenes **2**



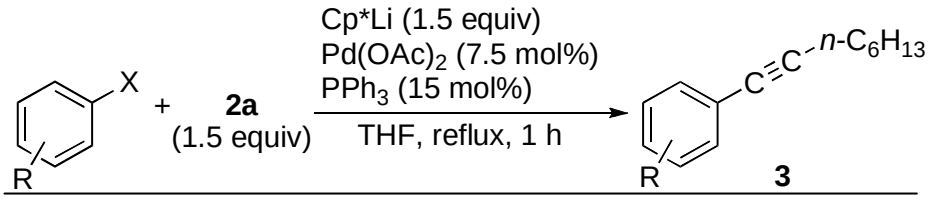
1 **2** (1.5 equiv) **3**

entry	R^1	R^2	isolated yield /%
1	H (**1a**)	*n*-C_6H_{13} (**2a**)	82 (**3aa**)
2	**1a**	*c*-C_6H_{11} (**2b**)	85 (**3ab**)
3	**1a**	Ph (**2c**)	93 (**3ac**)[a]
4	**1a**	TES (**2d**)	69 (**3ad**)[b]
5	**1a**	TMS (**2e**)	72 (**3ae**)[a,b]
6	*p*-Me (**1b**)	**2a**	81 (**3ba**)
7	*p*-OMe (**1c**)	**2a**	82 (**3ca**)
8	*p*-CF_3 (**1d**)	**2a**	70 (**3da**)
9	*p*-Cl (**1e**)	**2a**	71 (**3ea**)
10	*p*-COOEt (**1f**)	**2a**	83 (**3fa**)
11	*p*-CN (**1g**)	**2a**	74 (**3ga**)
12	*m*-Me (**1h**)	**2a**	83 (**3ha**)
13	*o*-Me (**1i**)	**2a**	83 (**3ia**)[c]
14	1-iodonaphthalene (**1j**)	**2a**	67 (**3ja**)

[a] 15 mol% of triphenylphosphine was added. [b] The reaction was carried out at 50 ˚C for 2 h. [c] The reaction was carried out for 1.5 h.

Not only aryl iodides but also aryl bromides, triflate, or nonaflate could be used as substrates in the Cp*-mediated reaction (Table 3). In these cases, the coexistence of triphenylphosphine was essential as a ligand.

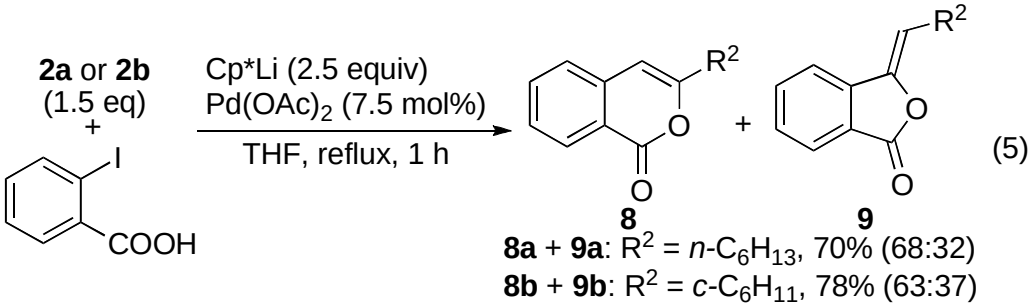
Table 3. Reactions of Various Aryl Bromides, Triflate or Nonaflate with 1-Octyne (**2a**)

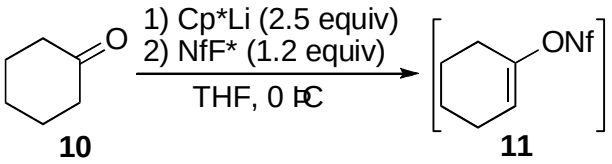


entry	X	R	isolated yield /%
1	Br	H	79 (**3aa**)
2	Br	*p*-OMe	74 (**3ca**)[c]
3	Br	*p*-CF_3	79 (**3da**)
4	OTf[a]	H	58 (**3aa**)
5	ONf[b]	H	88 (**3aa**)[c]

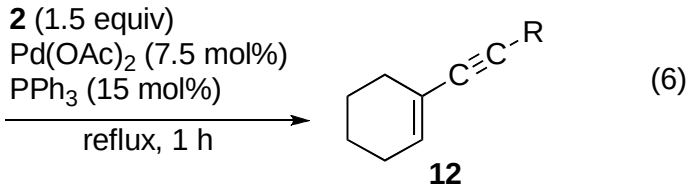
[a] Tf = trifluoromethanesulfonyl [b] Nf = 1,1,2,2,3,3,4,4,4-nonafluoro-1-butanesulfonyl [c] The reaction was carried out for 1.5 h.

By utilizing the advantages of Cp*Li as a base, the author finds two applications. The reaction of 2-iodobenzoic acid with **2** provided isocoumarin **8** and (*Z*)-3-alkylidenephthalide **9** in good yields (eq. 5).[5] He also found that Cp*Li can be used as a bulky base to prepare lithium enolates. With this reactivity, he accomplished one-pot synthesis of enynes **12** from ketone **10** *via* nonaflate **11** in good yields (eq. 6).





10 **11**



(6)

12

12a: R = *n*-C_6H_{13}, 64%
12b: R = Ph, 70%
12c: R = TMS, 69% (50 °C, 2 h)

*NfF = 1,1,2,2,3,3,4,4,4-nonafluoro
-1-butanesulfonyl fluoride

Experimental Section

General Procedure for Palladium-Catalyzed Cross-Coupling Reaction of Aryl Iodides with Terminal Acetylenes Using Cp*Li

A solution of butyllithium in hexane (1.60 M, 0.47 mL, 0.75 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.13 mL, 0.80 mmol) in THF (5 mL) at 0 ˚C. The mixture was stirred for 10 min at the same temperature. $Pd(OAc)_2$ (8.4 mg, 0.038 mmol), **2a** (82.7 mg, 0.75 mmol) in THF (0.5 mL), and **1a** (102 mg, 0.50 mmol) in THF (0.5 mL) were added to the reaction mixture. The resulting mixture was stirred for 1 h at reflux. The reaction mixture was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with hexane. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane) to afford **3aa** (75.5 mg, 0.41 mmol, 82%).

Preparation of Phenyl 1,1,2,2,3,3,4,4,4-nonafluoro-1-butanesulfonate

A solution of butyllithium in hexane (1.60 M, 3.44 mL, 5.5 mmol) was added to a solution of phenol (471 mg, 5.0 mmol) in THF (17 mL) at 0 ˚C. The mixture was stirred for 10 min at the same temperature. 1,1,2,2,3,3,4,4,4-Nonafluoro-1-butanesulfonyl fluoride (1.81 g, 6.0 mmol) in THF (1 mL) was added to the reaction mixture, and the mixture was stirred for 30 min at room temperature. The reaction was quenched with water, and the mixture was extracted with ethyl acetate. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane - ethyl acetate = 40:1) to afford phenyl 1,1,2,2,3,3,4,4,4-nonafluoro-1-butanesulfonate (1.52 g, 4.0 mmol, 81%).

General Procedure for Palladium-Catalyzed Cross-Coupling Reaction of Aryl Bromides, Triflate, or Nonaflate with 1-Octyne Using Cp*Li

A solution of butyllithium in hexane (1.60 M, 0.47 mL, 0.75 mmol) was added to a

solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.13 mL, 0.80 mmol) in THF (5 mL) at 0 ˚C. The white suspension was stirred for 10 min at the same temperature. $Pd(OAc)_2$ (8.4 mg, 0.038 mmol), triphenylphosphine (19.7 mg, 0.075 mmol), 1-octyne (82.7 mg, 0.75 mmol) in THF (0.5 mL), and bromobenzene (78.5 mg, 0.50 mmol) in THF (0.5 mL) were added to the reaction mixture, and the mixture was stirred for 1 h at reflux. The reaction was terminated with saturated aqueous NH_4Cl, and the mixture was extracted with hexane. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. Chromatographic purification on silica gel (Wakogel C-200, hexane) afforded **3aa** (73.4 mg, 0.39 mmol, 79%).

General Procedure for Palladium-Catalyzed Annulation of 2-Iodobenzoic Acid with Terminal Acetylenes Using Cp*Li

A solution of butyllithium in hexane (1.60 M, 0.78 mL, 1.25 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.20 mL, 1.3 mmol) in THF (5 mL) at 0 ˚C. The mixture was stirred for 10 min at 0 ˚C. $Pd(OAc)_2$ (8.4 mg, 0.038 mmol), **2a** (82.7 mg, 0.75 mmol) in THF (0.5 mL), and 2-iodobenzoic acid (124 mg, 0.50 mmol) in THF (0.5 mL) were added to the reaction mixture, and the mixture was stirred for 1 h at reflux. After being quenched with water, the mixture was extracted with ethyl acetate. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. Usual workup followed by purification on silica gel (Wakogel C-200, hexane - ethyl acetate = 20:1) gave mixture of **8a** and **9a** (**8a**:**9a** = 68:32, 80.8 mg, 0.35 mmol, 70%).

General Procedure for Palladium-Catalyzed One-Pot Synthesis of Enynes 12 from 10 *via* 11

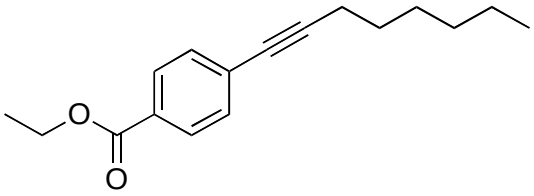
A solution of butyllithium in hexane (1.60 M, 0.78 mL, 1.25 mmol) was added to a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (0.20 mL, 1.3 mmol) in THF (5 mL) at 0 ˚C. The mixture was stirred for 20 min at the same temperature. Cyclohexanone (49.1 mg, 0.5

mmol) in THF (0.5 mL) was added to a white suspension, and the mixture was stirred for 30 min at 0 ˚C. 1,1,2,2,3,3,4,4,4-Nonafluoro-1-butanesulfonyl fluoride (181 mg, 0.60 mmol) in THF (0.5 mL) was added to the reaction mixture, and the mixture was stirred for 30 min at 0 ˚C. 1-Octyne (**2a**, 82.7 mg, 0.75 mmol) in THF (0.5 mL), triphenylphosphine (19.7 mg, 0.075 mmol), and $Pd(OAc)_2$ (8.4 mg, 0.038 mmol) were added to the reaction mixture, and the mixture was stirred for 1 h at reflux. Water was added to quench the reaction, and the mixture was extracted with hexane. The combined organic parts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. The oil was purified by chromatography on silica gel (Wakogel C-200, hexane) to afford **12a** (60.3 mg, 0.32 mmol, 64%).

Characterization Data

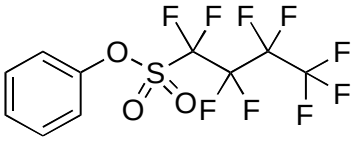
The compounds **3aa**, **3ac**, and **3ae** are commercially available. The products **3ab**,[6] **3ad**,[7] **3ba**,[8] **3ca**,[8] **3da**,[8] **3ea**,[9] **3ga**,[8] **3ha**,[8] **3ia**,[8] **3ja**,[10] **12a**,[11] **12b**,[12] and **12c**[12] can be found in the literature.

Ethyl 4-(1-octynyl)benzoate (3fa)



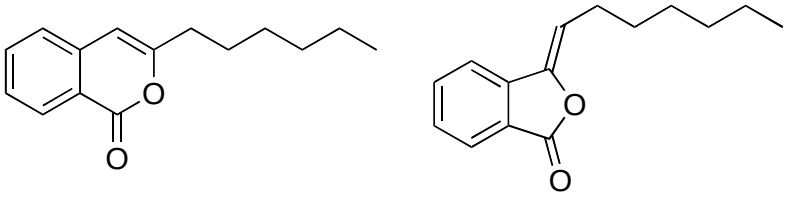
IR (neat) 2932, 2859, 1720, 1608, 1466, 1367, 1306, 1272, 1175, 1106, 1097, 1021, 857, 770, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, *J* = 7.0 Hz, 3H), 1.28–1.64 (m, 8H), 1.39 (t, *J* = 7.0 Hz, 3H), 2.42 (t, *J* = 7.0 Hz, 2H), 4.36 (t, *J* = 7.0 Hz, 2H), 7.41–7.45 (m, 2H), 7.93–7.97 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.04, 14.30, 19.50, 22.53, 28.54, 28.60, 31.33, 61.01, 80.12, 93.90, 128.81, 129.13, 129.33 (× 2), 131.39 (× 2), 166.20. Found: C, 78.92; H, 8.78%. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58%.

Phenyl 1,1,2,2,3,3,4,4,4-nonafluoro-1-butanesulfonate



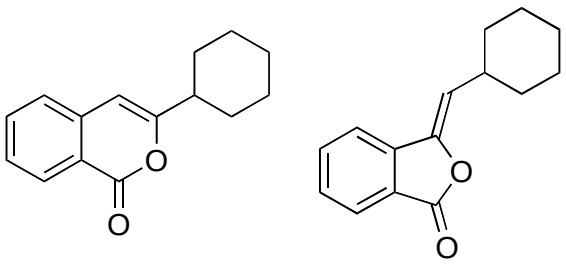
IR (neat) 1488, 1427, 1354, 1230, 1204, 1145, 1133, 1036, 891, 772, 686 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.28–7.31 (m, 2H), 7.37–7.42 (m, 1H), 7.44–7.48 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 107.44–118.48 (m, × 4), 121.35 (× 2), 128.35, 130.25 (× 2), 149.89. Found: C, 31.87; H, 1.50%. Calcd for $C_{10}H_5F_9O_3S$: C, 31.93; H, 1.34%.

3-Hexylisocoumarin (7a) and (*Z*)-3-Heptylidenephthalide (8a) (68:32)



IR (neat) 2929, 2857, 1782, 1733, 1658, 1484, 1161, 1024, 983, 759, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J* = 7.5 Hz, 3H), 1.24–1.74 (m, 8H), 2.47 (dt, *J* = 7.5, 7.5 Hz, 2 × 0.32H), 2.52 (t, *J* = 7.5 Hz, 2 × 0.68H), 5.64 (t, *J* = 7.5 Hz, 1 × 0.32H), 6.25 (s, 1 × 0.68H), 7.32–8.27 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 14.01, 14.05, 22.49, 22.56, 25.81, 26.85, 28.66, 28.96, 29.22, 31.48, 31.60, 33.51, 102.82, 109.76, 119.59, 120.10, 124.43, 124.98, 125.22, 127.49, 129.27, 129.48, 134.17, 134.67, 137.63, 139.58, 145.58, 158.33, 163.11, 167.21. Found: C, 78.13; H, 7.83%. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88%.

3-Cyclohexylisocoumarin (7b) and (*Z*)-3-Cyclohexylmethylenephthalide (8b) (63:37)



IR (nujol) 1776, 1727, 1718, 1649 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28–2.08 (m, 10H), 2.41–2.48 (m,

1 × 0.63H), 2.79–2.88 (m, 1 × 0.37H), 5.50 (d, J = 9.5 Hz, 1 × 0.37H), 6.23 (s, 1 × 0.63H), 7.34–8.27 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 25.63, 25.86 (× 3), 25.92 (× 2), 30.56 (× 2), 32.85 (× 2), 35.28, 41.84, 100.85, 115.04, 119.64, 120.26, 124.37, 125.20, 125.22, 127.45, 129.27, 129.42, 134.15, 134.60, 137.74, 139.78, 144.16, 162.35, 163.12, 167.25. Found: C, 79.13; H, 7.20%. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06%. m.p. 78.0–79.0 ˚C.

References and Notes

(1) Initial examples of the synthesis of Cp*-metal complexes: (a) R. B. King, M. B. Bisnette, *J. Organomet. Chem.* **1967**, *8*, 287. (b) H. Röhl, E. Lange, T. Gößl, G. Roth, *Angew. Chem.* **1962**, *74*, 155.

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Publication List

I. Parts of the present thesis have been published in the following journals.

Chapter 1 Minoru Uemura, Hideki Yorimitsu, and Koichiro Oshima
Tetrahedron Lett. **2006**, *47*, 163–166.
Minoru Uemura, Kazunari Yagi, Masayuki Iwasaki, Kenichi Nomura, Hideki Yorimitsu, and Koichiro Oshima
Tetrahedron **2006**, *62*, 3523–3535.

Chapter 2 Minoru Uemura, Hideki Yorimitsu, and Koichiro Oshima
Chem. Lett. **2006**, *35*, 408–409.

Chapter 3 Masayuki Iwasaki, Eiji Morita, Minoru Uemura, Hideki Yorimitsu, and Koichiro Oshima
Synlett **2007**, 167–169.
Minoru Uemura, Masayuki Iwasaki, Eiji Morita, Hideki Yorimitsu, and Koichiro Oshima
Bull. Chem. Soc. Jpn. **2007**, *80*, 2400–2405.

Chapter 4 Minoru Uemura, Hideki Yorimitsu, and Koichiro Oshima
Chem. Commun. **2006**, 4726–4728.

Chapter 5 Minoru Uemura, Hideki Yorimitsu, and Koichiro Oshima
Tetrahedron in press.

II. Other publications not included in this thesis.

(1) Highly Practical and General Synthesis of Monodisperse Linear π-Conjugated Oligoenynes and Oligoenediynes with Either *trans*- or *cis*-Olefin Configuration
Yuuki Takayama, Christophe Delas, Kenji Muraoka, Minoru Uemura, and Fumie Sato
J. Am. Chem. Soc. **2003**, *125*, 14163–14167.

(2) Site-Selective Pd-Catalyzed Coupling of 1,4-Diiodo-1,3-Alkadienes with Grignard Reagents, and Its Application to Synthesis of Fulvenes
Minoru Uemura, Yuuki Takayama, and Fumie Sato
Org. Lett. **2004**, *6*, 5001–5004.

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Minoru Uemura